2.1 Introduction

Delirium is a common medical condition that healthcare providers will encounter while caring for older adults, especially in the hospitalized patient. On a general medical service, rates of delirium range from 10 to 40% [1–3]. Further, up to a quarter of hospitalized patients over age 65 will present with delirium [4]. An additional 30% of hospitalized patients in this age group will develop delirium acutely during their hospitalization [5]. Familiarity with the clinical syndrome of delirium, identification of which patients are at risk, and knowledge on how to prevent, diagnose, and treat delirium are critical to healthcare professional’s ability to provide high quality care of hospitalized older adults.

Delirium is critical to prevent and, should it occur, to recognize early because of its close association with increased morbidity and mortality in the hospitalized patient. Patients who experience delirium have long-term loss of cognitive function, higher complication rates, increased hospital length of stay, and higher mortality. Delirium has recently been recognized as a complex phenotype in older patients that shifts the prevalence focus from chronologic age and medical comorbidities to the functional impact of comorbidities especially frailty (discussed fully in a separate chapter) and disability. While the frail older adult is at higher risk for delirium in the hospitalized setting, any hospitalized patient can develop delirium.

2.2 Delirium Definition

Delirium is defined as a disturbance in attention and awareness, with a change in cognition that occurs over a short period of time (hours to days) and fluctuates during the course of the day. Differentiating preexisting dementia from delirium is critically important. Clinically, delirium presents with inattention, disordered thinking, and loss of orientation, with a component of both agitation and hyperactivity, or, especially in the elderly, with depressed affect and hypoactivity. Patients can appear confused, have hallucinations, be somnolent, or present with all of these symptoms during the course of delirium. Unlike dementia, delirium waxes and wanes over the course of the day, so patients may have normal behavior during one assessment, and be agitated or somnolent the next. Thus, a high level of clinical suspicion is necessary in order to recognize and diagnose a patient with delirium. The hypoactive delirium subtype is widely recognized as the most under-diagnosed presentation of delirium.

2.3 Delirium Risk Factors

The risk of developing delirium following surgery is best described as a relationship between a physiologic stressor, predisposing patient risk factors, and iatrogenic conditions (see Fig. 2.1) [6]. A multitude of risk factors have been identified that increase the chances of the development of delirium; this multiplicity includes both intrinsic patient factors and external precipitating factors during a hospital stay. Risk factors for delirium are multifactorial, and there is a dose-response to the number of risk factors and the odds of developing delirium [7]. Dementia is the most closely associated intrinsic patient vulnerability that increases risk of delirium [8, 9]. The greater the severity of dementia, the greater the risk of developing delirium [10]. Patients with underlying medical conditions associated with frailty such as poor mobility, fatigue, a high level of co-morbid medical conditions [11], and malnutrition [12] also place patients at
risk for development of delirium [13]. Frail patients can have rates of delirium of up to 60% [4]. Other intrinsic risk factors include increased age and sensory impairment (visual or hearing) [7].

Routine hospital care introduces external iatrogenic risk factors, including polypharmacy (discussed fully in a separate chapter), disruption of sleep–wake cycles, infection, psychoactive medication prescription (specifically benzodiazepines and anti-cholinergic drugs), physical restraints, use of bladder catheters, and iatrogenic adverse events have all been identified as risk factors for delirium [14]. See Table 2.1 for a summary of delirium risk factors.

Various specialty-specific rates of delirium have been reported that further identify groups of hospitalized patients who are more at risk for the development of delirium. Patients who present to the emergency department or are in the intensive care unit, oncology patients, and patients for multiple surgical specialties (e.g., vascular or orthopedic surgery) can have higher rates of delirium than the average hospitalized adult. Ten percent of patients present to the emergency department with delirium, although this number may under-represent the true incidence [13, 15]. Orthopedic injuries and operations also carry high risk, with 40% of patients developing delirium after bilateral knee replacement [16] and up to 60% following hip fracture [17]. Patients undergoing coronary artery bypass grafting have rates of postoperative delirium of 33–50% [18, 19].

Intensive care unit (ICU) patients, both medical and surgical, are at extremely high risk of delirium. The prevalence of delirium has been reported to be as high as 80% [20]. There is, however, dramatic variability in the incidence of delirium in the ICU. Recently, because of the recognition of the risk of delirium, many ICUs have specific pathways for delirium prevention, which can significantly reduce the

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**Table 2.1** Risk factors for delirium

<table>
<thead>
<tr>
<th>Extrinsic Factors</th>
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<tr>
<td>Low illness severity</td>
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<tr>
<td>Minor surgical stress</td>
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<tr>
<td>Intrinsic Factors</td>
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<tr>
<td>Low vulnerability</td>
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<tr>
<td>Iatrogenic Factors</td>
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<td>Low hospital driven stress</td>
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**Fig. 2.1** Multifactorial model of delirium. The risk of a delirium is a combination of extrinsic factors to the patient (e.g., severity of medical illness, stress of surgical intervention), intrinsic factors to the patient (e.g., cognitive impairment, advanced age), and iatrogenic factors (e.g., sleep disruption, pain control).
occurrence of delirium [21, 22]. ICU care is associated with disruption of sleep–wake cycling, high severity of illness, and use of many drugs that are associated with increased risk of delirium, so it is unsurprising these patients are more vulnerable to developing delirium.

### 2.4 Presentation of Delirium

Delirium is exceptionally heterogeneous in its presentation. The fact that the course of delirium waxes and wanes makes the diagnosis of delirium clinically challenging. This has led to a wide variety of diagnostic tools which can be used to diagnose delirium (see “Diagnostic Tools” section below and Chap. 8, Screening Tools for Geriatric Assessment by Specialists).

While there are several ways to define subtypes of delirium, one of the most commonly used strata is by motor activity, known as hyperactive, hypoactive, and mixed subtypes of delirium (see Fig. 2.2) [23]. The primary distinction between these motor subtypes is the presence of agitation versus lethargy in the patient’s clinical presentation. Patients with evidence of both hyperactive and hypoactive delirium are described as having mixed delirium.

There are several checklists (see section below) that identify psychomotor symptoms that are associated with delirium, and when present in combination, increase the specificity of these symptoms to delirium [24]. Hyperactivity in delirium may be associated with increased involuntary movements, restlessness, wandering, increased speed, amount, or volume of speech, inability to sleep, distractibility, combativeness, hallucinations, or tangential thoughts (among others). Hypoactive delirium may present as apathy, decreased activity, decreased speed, amount, or volume of speech, somnolence, or decreased alertness. A mixed subtype presentation occurs when patient symptoms fluctuate between these two categories of agitation and lethargy.

Hypoactive delirium may be under-represented in the epidemiology of delirium because it is difficult to diagnose [25, 26]. A high level of clinical vigilance and suspicion of the diagnosis of delirium is especially necessary to diagnose hypoactive delirium. Hypoactive symptoms may be easy to attribute to other patient health conditions without a high clinical suspicion to monitor for delirium. Further, some studies have demonstrated that postoperative patients with hypoactive delirium have worse prognosis when monitoring 6-month mortality rate [27], although other studies have demonstrated improved outcomes for patients with hypoactive delirium [28].

### 2.5 Diagnostic Tools for Delirium

There are many diagnostic tools to identify delirium. They can be specifically designed for the ICU patient or other clinical settings, and may focus on certain diagnostic criteria, such as motor subtype. Below are brief descriptions of some commonly used diagnostic tools and comments about specific indications or limitations.

The confusion assessment method (CAM) is the most widely recognized tool to assess delirium and can be completed in under 5 min. [29] It uses four criteria: (1) acute onset of symptoms with fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered level of consciousness. The first 2 criteria must be present with either the 3rd or the 4th criteria. It has high inter-rater reliability with high accuracy compared to psychiatrist assessment for delirium.

The Delirium Rating Scale-Revised-98 (DRS-R98) is a 16-item scale, of which 13 items score for severity of symptoms. It has high inter-rater reliability, sensitivity, and specificity, including use in patients who have concomitant neurologic disease, such as dementia [30]. It is designed for use by any healthcare professional.

The cognitive test for delirium (CTD) is a diagnostic test specifically designed to assess critically ill hospitalized patients, including patients unable to communicate, such as those who are intubated and sedated [31]. It particularly emphasizes nonverbal domains, specifically visual and auditory symptoms. It is also able to reliably distinguish the difference between delirium and other psychiatric disorders.
The Delirium Motor Subtype Scale (DMSS) is used specifically to identify features of hyperactive and hypoactive delirium [24]. It is an 11-point scale any healthcare provider can use to assess patient behaviors, and includes 7 hypoactive features and 4 hyperactive features. Two symptoms must be present in order to classify delirium in a specific subtype.

The CAM for the Intensive Care Unit (CAM-ICU) was developed from the CAM assessment to better diagnose patients who are mechanically ventilated [32]. It uses non-verbal assessments to identify the same criteria of acute onset of symptoms with fluctuating course, inattention, and disorganized thinking or altered level of consciousness. It has high levels of sensitivity and specificity for delirium in ventilated patients, although the traditional CAM is more effective in patients able to fully participate in the assessment [20].

The intensive care delirium screening checklist is another test for patients in the ICU setting. It is a brief checklist of eight items based off of DSM criteria of delirium [33]. While it also has high sensitivity for delirium in the ICU, it is less specific than the CAM-ICU method. It is designed for use for all healthcare professionals.

The Memorial Delirium Assessment Scale was specifically developed to monitor development of delirium in ill patients enrolled in clinical trials [34]. It involves a 10-item checklist which was validated in patients with AIDS and metastatic cancer. It is well suited for use in repeated assessments over time for patients being seen longitudinally in trials.

The important issue is that a clinician should be very familiar with one or two of these screening tools and use them in daily practice.

### 2.6 Medical Evaluation of Delirium

Given the heterogeneous presentation of the clinical syndrome of delirium in combination with the complex intrinsic and iatrogenic precipitating factors, a structured, thorough, and routine approach to evaluation of the patient with delirium is necessary. A hospitalized patient may have presented at admission with delirium or develop it during their hospital course. While it is not only important to recognize the clinical syndrome, it is also important to identify correctable conditions which contributed to the state of delirium. Acute onset of delirium may have developed secondary to a single provocative factor (such as a symptomatic urinary tract infection (UTI), myocardial infarction (MI)), multiple medications (polypharmacy), admission to ICU, and others).

The appropriate workup of delirium involves methodical evaluation of the patient to identify treatable causes as well as initiate behavioral interventions. Table 2.2 outlines a comprehensive workup for patients with acute delirium which should supplement bedside examination. While many of these tests should be considered to be routine in an acute clinical change, others should only be considered if clinically indicated.

### 2.7 Prevention of Delirium

Although recognition and treatment of delirium once the patient develops the syndrome is essential, interventions to prevent delirium occurrence are essential for all patients at risk for delirium. Identification of individuals with multiple

<table>
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<tr>
<th>Table 2.2 Medical evaluation of delirium</th>
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<tbody>
<tr>
<td><strong>Routinely ordered</strong></td>
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<tr>
<td><strong>Laboratory tests</strong></td>
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<tr>
<td>Complete blood count (infection, anemia)</td>
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<tr>
<td>Basic metabolic panel (electrolyte disturbances, acid base status, renal function)</td>
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<td>Glucose (hypo- or hyper-glycemia)</td>
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<tr>
<td>Arterial blood gas (hypoxia or hypercarbia)</td>
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<tr>
<td>Urine analysis (infection but asymptomatic bacteriuria is not thought to cause delirium and is very common in older patients, especially women)</td>
</tr>
<tr>
<td><strong>Imaging</strong></td>
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<tr>
<td>Chest X-ray (infection)</td>
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<td></td>
</tr>
<tr>
<td><strong>Clinical evaluation</strong></td>
</tr>
<tr>
<td>Physical examination</td>
</tr>
<tr>
<td>Medication review (BEERs list)</td>
</tr>
<tr>
<td>Social history (alcohol or benzo use)</td>
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<tr>
<td><strong>Ancillary tests</strong></td>
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<tr>
<td>EKG (myocardial infarction)</td>
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<tr>
<td>Pulse oximetry (hypoxia)</td>
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risk factors (e.g., frail, elderly, multiple comorbidities) allows the clinician to target preventive interventions to the at-risk population. Interventions such as making sure the patient has full use of their sensory aids, orientation protocols, early mobilization measures, minimization of sleep disturbance, and avoidance or discontinuation of high risk medications can all create an environment that will lower the risk of delirium for the at-risk patient [35]. Daily rounds that address these non-pharmacologic interventions utilize a multidisciplinary care team and plan that creates consistent assessment of these issues. Up to 40% of hospitalized patients may have preventable delirium [14, 28]. Both of the current clinical practice guideline statements strongly recommend the implementation of multi-component delirium prevention protocols for patients at risk for delirium [35, 36].

Educational programs concerning delirium in every medical center are essential. These programs should be considered a system-level prevention tool. Education of healthcare providers about recognition, prevention, and treatment of delirium consistently reduces episodes of and duration of delirium, regardless of the specific intervention or protocol. [37–39] Further, educational interventions are cost-effective and associated with no patient harm [40–42].

2.8 Treatment of Delirium

When a patient does develop acute delirium, management of a potential underlying reversible cause of the delirium is essential. Appropriate treatment of identifiable causes will improve the patient’s clinical condition. However, risks and benefits of aggressive or interventional therapies should be considered when treating a delirious patient, and weighed in the context of their clinical condition and goals of care. See Table 2.3 for modifiable causes of delirium with a proposed intervention. Behavioral modifications have been described above in the section regarding prevention of delirium. Interventions such as encouraging use of sensory aids, establishing day–night cycling, and the other interventions described in the previous section are effective in treating delirium in addition to their role in prevention.

Multiple pharmacologic interventions have been explored both as prophylaxis of delirium and as treatment. At this time, pharmacologic prophylaxis of delirium is not recommended. There are very few randomized, controlled trials exploring pharmacologic prophylaxis. Prophylactic use of epidural anesthesia, donepezil, and tryptophan administration has not been associated with a significant change in incidence or duration of delirium [43–45]. Prophylactic haloperidol is associated with no difference in the incidence of delirium, but has been associated with shorter duration of delirium and hospital length of stay in patients who were identified as being high risk for delirium [46]. Prophylactic haloperidol, however, is not recommended as this drug has its own serious side effects. Melatonin has been found to reduce delirium in both medical and surgical hospitalized patients but these data are not robust enough to recommend its routine use [47, 48].

Pharmacologic treatment of delirium should be reserved only for patients who have failed behavioral interventions and are at significant harm to themselves or others. Pharmacologic treatment typically is an antipsychotic, such

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<th>Table 2.3</th>
<th>Factors that cause delirium which can be clinically addressed</th>
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<tbody>
<tr>
<td>Modifiable delirium trigger</td>
<td>Clinical intervention</td>
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| Immobility | • Ambulate in hallway three times daily  
• Early physical therapy consultation |
| Sensory impairments | • Glasses accessible at beside  
• Hearing aids accessible at beside |
| Impaired cognition | • Orientation three times daily  
• Family/friends at bedside |
| Medications | • Avoid high risk medications/polypharmacy  
• Daily medication review |
| Dehydration | • Assess and manage volume status  
• Adequate hydration |
| Pain | • Proactively assess and manage pain  
• Use non-opioid meds if possible |
| Nutrition | • Proactively encourage nutrition  
• May require swallowing evaluation |
| Sleep enhancement | • Allow overnight sleep without interruption  
• Reduce nighttime noise |
| Respiratory status | • Assess and manage hypoxia  
• Assess and manage hypercarbia |
| Infection | • Recognize delirium as presentation of infection  
• Work-up infection in delirium evaluation |
| Iatrogenic causes | • Remove unnecessary catheters/lines  
• Avoid dark daytime room |
as haloperidol, but this treatment should not be universal and is not without risk. There is significant heterogeneity in the study designs and interventions observed in studies on the pharmacologic treatment of delirium. Antipsychotics are associated with adverse outcomes such as an increase in mortality and motor side effects, including the neuroleptic malignant syndrome. Nonetheless, haloperidol or other antipsychotics have been used for severe agitated delirium only when behavioral interventions have failed and there is concern for patient safety or that of others [35]. Antipsychotic use in the treatment of delirium may improve the symptoms of agitation but does nothing for underlying delirium pathophysiology. If ever prescribed, the clinician should have a plan for tapering and discontinuing antipsychotics as soon as possible and typically within a few days. Benzodiazepines are contraindicated in treatment of the delirious patient and can actually exacerbate and prolong an acute episode of delirium [49].

2.9 Outcomes of Delirium

Delirium is not only a common condition in the hospitalized and elderly patient, it is associated with significantly worse long-term clinical outcomes for patients. Delirium has been associated as an independent predictor of increased morbidity and mortality across multiple patient groups, including postoperative patients (gastrointestinal, cardiac, and orthopedic), ICU patients, and cancer patients.

In a broad variety of surgical patients, delirium is associated with significant increases in 30-day mortality [50, 51]. It has also been associated with increased 6-month mortality in general surgery and thoracic surgery patients [27]. ICU patients similarly have worsened 6-month survival if they suffered from delirium, independent of other conditions [20].

Delirium is also associated with increased morbidity in addition to increased mortality. Delirium is independently associated with increased ICU length of stay, hospital length of stay, and rate of discharge to an institutional facility [27, 50, 51]. These outcomes, especially the loss of independence with institutional discharge, may be of critical importance to patients and families when discussing prognosis and goals of care in the hospitalized patient with delirium.

2.10 Conclusion

Delirium is a common clinical syndrome in the hospitalized patient, with increasing rates in vulnerable populations, such as the frail, patients with multiple comorbidities, and those in the ICU. Delirium is a clinically heterogeneous condition, with psychomotor changes that can range from extreme agitation that endangers patient and provider safety, to subtle lethargy that can be difficult to clinically detect. The most effective prevention and treatment of delirium involves multifactorial and multidisciplinary behavioral modifications and medical optimization of underlying conditions. There is no consensus about uniformly effective pharmacologic prophylaxis or treatment. Delirium is a high risk condition, which is associated with increased morbidity and mortality, and is a critical syndrome for all healthcare providers to recognize.

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