

Delirium in the Elderly: A Review

Suzanne Wass,¹ Penelope J. Webster,² Balakrishnan R. Nair³

Abstract

Delirium is a common disorder, often under diagnosed and mismanaged. It is becoming more prevalent, because of the ageing population. In this clinical review, we summarise the definition, diagnosis and management of delirium.

Keywords: Delirium, Dementia, Depression.

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From the Department of ¹Geriatric Medicine, Calvary Mater Hospital, NSW Australia,² Geriatric Medicine, John Hunter Hospital, NSW, Australia,³ Continuing Medical Professional Development, School of Medicine and Public Health, University of New Castle, and Continuing Professional Development, Hunter New England Health, NSW, Australia.

Address correspondence and reprint to: Prof. Balakrishnan R. Nair, MBBS, FRACP, FRCP Clinical Professor of Medicine, Associate Dean Continuing Medical Professional Development, School of Medicine and Public Health, Director of Continuing Professional Development, Hunter New England Health, NSW, Australia
Email: Kichu.Nair@newcastle.edu.au

Delirium is a common syndrome affecting many elderly patients not only admitted into acute medical wards but also in the community. The syndrome of delirium can be defined as acute brain failure associated with autonomic dysfunction, motor dysfunction and homeostatic failure. It is complex and often multi-factorial, and hence continues to be under diagnosed and poorly managed. Despite medical progress, delirium remains a major challenge for health care workers with the increasing burden of an ageing population.

Definition and Terminology

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) defines delirium as:

*“a disturbance of consciousness that is accompanied by a change in cognition that cannot be better accounted for by a pre-existing or evolving dementia”.*¹

Delirium develops over a short period of time (hours to days) and fluctuates throughout the course of the day. It is characterised by a reduction in clarity of awareness, inability to focus, distractibility and change in cognition. Other terminology used to describe delirium includes ‘acute confusional state’, ‘acute brain syndrome’, ‘acute organic reaction’, ‘acute brain failure’ and ‘post-op psychosis’.^{2,3}

Occurrence and consequences of delirium

The available data for the incidence and prevalence of delirium is varied. It appears that 15% to 30% of elderly patients will have delirium on admission to hospital and up to 56% will develop delirium during their stay.⁴ Incidence of delirium is highest amongst certain subgroups including those with cancer, AIDS and terminal illness and after surgical procedures such as hip replacement and cardiac surgery. It is more common in certain ward environments like ICU and palliative care units.⁵ The point

prevalence of delirium in the community is 1.1% amongst the general population aged over 55 years,⁶ and up to 14% in those over 85 years.⁷ The incidence amongst nursing home residents surpasses 60%.¹

The consequences of delirium are considerable for the patient and the health services. In the US delirium is estimated to increase health costs by US\$2500 per patient, totalling US\$6.9 billion per year.⁸ If we consider that less than half of patients have fully recovered at point of discharge, this incurs additional costs in the form of increased residential care, rehabilitation and home services.^{9,2}

Even when detected early and managed appropriately, delirium can lead to significant mortality and morbidity in frail, elderly patients. Adverse outcomes can include the following:

- Prolonged hospital stay (on average 8 days longer)¹⁰
- Increased mortality whilst in hospital (up to 75%) in the months following Discharge (40% 1 year mortality)^{1,11,12,13}
- Increased risk of developing complications such as hospital acquired infection; pressure ulcers, incontinence and falls (despite the use of restraints)^{14,15}
- Poor physical and cognitive recovery at 6 and 12 months,¹⁵ with lower scores on the Mini Mental State Examination (MMSE) at discharge compared to controls¹⁶
- Increased risk of placement in a residential home^{1,13}
- Increased risk of developing dementia even in patients with no cognitive impairment at baseline¹⁷

The odds of a poor outcome are increased by the frailty of the patient and delays in diagnosis,¹⁵ highlighting the crucial importance of early detection and proactive management.

Classification

The DSM-IV-TR classifies delirium according to aetiology, as follows:

1. Delirium due to a general medical condition
2. Substance Intoxication Delirium (drugs of abuse)
3. Substance Withdrawal Delirium
4. Substance Induced Delirium (medications or toxins)
5. Delirium due to Multiple Etiologies
6. Delirium not otherwise specified.

Clinically delirium can be divided into the following three categories:

- i. **Hyperactive Delirium** (30%). Patients are agitated and hyper alert with repetitive behaviours, wandering, hallucinations and aggression. Although recognised earlier, there is association with increased use of benzodiazepines, over sedation, use of restraints and falls.
- ii. **Hypoactive Delirium** (25%). Patients are quiet and withdrawn which is often missed on a busy medical ward leading to increased length of stay, increased and more severe complications.
- iii. **Mixed Delirium**. Fluctuating pattern seen in 45% of cases.^{3, 10, 14, 18}

Clinical features

The DSM-IV-TR stipulates that, as well as matching the definition, patients must have the following clinical features:

1. *Disturbance of consciousness*. A reduced ability to focus, inattention and reduced awareness of the environment.
2. *A change in cognition* or perceptual disturbance including memory deficits, disorientation and language disturbance.
3. The above features develop over hours to days and fluctuate throughout the day.^{1,10}

There are many other features that can be associated with delirium and these are described in Table 1. It is also worth remembering that frank delirium can be preceded by a period of prodromal illness (normally 1-3 days), where the patient may appear impatient, anxious, restless, distracted, develop urinary incontinence or start refusing investigations. In hindsight, family members are able to give a history of this prodromal period but it is very difficult to detect clinically. Elderly patients with delirium often do not look ill apart from the behavioural changes.

Table 1: Clinical Features of Delirium

Essential Features	Variable Features
Acute onset	Perceptual disturbance
Fluctuating course	Hyper/hypoactive
Inattention	Altered sleep/wake cycle
Disorganised thinking and speech	Emotional disturbance
Clouding of consciousness	
Cognitive deficit	
Examination Signs	Autonomic Dysfunction
Dysarthria	Tachycardia
Dysnomia	Hypertension
Dysgraphia	Sweating
Aphasia	Flushing
Nystagmus	Dilated pupils
Ataxia	
Tremor/ Asterixis	
Myoclonus	

Adapted from Inouye SK. Delirium in Older Persons. NEJM; 354:1157-65

Risk and Precipitating Factors

Most elderly patients will have multiple risk factors making them more susceptible to delirium (see Table 2). Vulnerability is also increased when multiple precipitating factors are present, or if the precipitating insult is particularly severe. It is impossible to list all of the conditions and stressors that may precipitate delirium, but the most common (and most relevant to an elderly population) are listed in Table 3. Delirium is often the only sign of an underlying serious medical illness in an elderly patient and, therefore, particular attention should be made to identifying and correcting these factors if at all possible.

Table 2: Common Risk Factors for Delirium

Non Correctable
Age
Male
Mild Cognitive Impairment, Dementia, Parkinson's Disease present in >50% of patients. ¹⁹
Multiple co-morbidities including:
• Renal and hepatic disease
• History of CVA
• History of falls and poor mobility
• History of prior delirium.

Correctable
Hearing impairment or visual impairment indicates a threefold risk. ²⁰
Malnutrition, dehydration, low albumin. Associated with a twofold risk. ²⁰
Social Isolation, sleep deprivation, new environment, moves within the hospital. ¹²¹
Restraints and indwelling catheters
New addition of three or more medications
No time orientation
Smoking
Potentially Correctable
Uraemia, blood urea >10 is an independent risk factor. ²²
Depression
Prolonged hospital stay, increased risk after 9 days. ⁵
CVA: Cerebrovascular Accident

Table 3: Precipitating Factors

Precipitating Factors
Prescribed medication and polypharmacy
Alcohol withdrawal and benzodiazepines
Sepsis, shock, hypothermia
Electrolyte disturbance (sodium, calcium, magnesium, phosphate)
Endocrine disturbance (Blood sugar, thyroid)
Nutritional deficiencies (thiamine, B12, folate)
Cardiac, liver or renal failure
Pulmonary disorders (particularly in the setting of hypoxemia)
CVA or seizures
Post surgery, especially cardiac, orthopaedic or with ICU stay
Falls and fractures
Anaemia or gastrointestinal bleed
Pain
Cancer and terminal illness
CVA: Cerebrovascular Accident

Recognising patients with delirium

When a patient with confusion is admitted to hospital, they should be presumed to have delirium until proven otherwise. A collaborative history from family or carers is essential to establish

the acute decline in cognition that needs to be taken into account during cognitive screening assessments. Studies show that 30% to 67% of patients with delirium go undetected.^{18, 24} Detection can be improved by implementing cognitive testing and screening instruments, accompanied by educational programmes for staff.²⁵

The MMSE is the most widely used instrument to test cognitive function. Although it is used in the setting of delirium, it was not designed for this purpose. To detect delirium, it is necessary to know the patients baseline function and engage the patient in repeat testing throughout their illness. This may be effective in certain high-risk situations (i.e. post hip fracture) but further evaluation is needed.²⁶ A drop of >2 points from baseline indicates delirium, whilst an improvement of 3 points or more indicates resolution.⁵

The Australian Society for Geriatric Medicine, The American Psychiatric Association and The British Geriatrics Society all recommend the Confusion Assessment Method (CAM), a screening tool specifically designed to detect delirium (see Table 4). This has reported sensitivity of >94%, specificity of >90% and is easy to use in a clinical setting. Again the patient should be reassessed throughout their hospital stay to monitor progress.¹⁴

Table 4: Confusion assessment Method (CAM)

Confusion assessment Method (CAM)
1. Acute onset and fluctuating course
<ul style="list-style-type: none"> Is there evidence of change in cognition from baseline? Does this fluctuate during the day?
2. Inattention
<ul style="list-style-type: none"> Does the patient have difficulty focusing attention? Do they seem distracted?
3. Disorganised thinking
<ul style="list-style-type: none"> Does the patient have disorganised thinking, rambling speech or seem incoherent?
4. Altered level of consciousness
Rate the level as follows:
<ul style="list-style-type: none"> Alert, hyper alert, lethargic or drowsy, stupor, coma
All patients must have 1 and 2 with either 3 or 4 to diagnose delirium
Adapted from Harrisons Online, Chapter 26. Confusion and Delirium, McGraw-Hill Companies.
Accessed February 2009.

The third assessment tool worth noting is the Delirium Rating Scale (DRS). It covers a range of symptoms relating to delirium, not only useful for diagnostic purposes, but for assessing severity

and distinguishing delirium from other disorders. Although accurate, it is more complex than the CAM, requires specialist trained Psychiatrists or Geriatricians and has mainly been used for research purposes until recently.²⁷

It is important to differentiate between delirium, dementia and depression. Lewy Body Dementia, with its hallucinations and fluctuations is a classic example, whilst 42% of patients referred to psychiatric services for depression actually have delirium.²⁸ Table 5 summarises the main differences.

Table 5: Differentiating between Delirium, Dementia and Depression

	Delirium	Dementia	Depression
Onset	Acute	Insidious	Variable
Course	Fluctuating	Progressive	Diurnal variation
Consciousness	Altered, clouded	Clear until late stages	Clear
Attention	Inattention	Normal	Poor
Memory	Poor short term memory	Poor short term Memory	Normal
Thinking	Disorganised, incoherent	Difficulty with abstract thought	Intact, low self worth, Hopelessness
Perception	Misinterpretation Hallucinations Delusions	Usually normal (except Lewy Body)	Can have complex delusions paranoid psychosis
MMSE	Distracted, difficulty completing MMSE	Struggles/Tries to find correct reply	Lacks motivation "I don't know"

MMSE: Mini Mental State examination

Adapted from Milisen K et al. Nurs Clin N Am. 2006; 41: 1-22

Prevention of delirium

Prevention can be divided into primary, secondary and tertiary. Primary prevention strategies are aimed at reducing the incidence of delirium. Given that delirium is a complex medical problem resulting from one or more variables involving body systems in addition to environmental factors, as delineated above, it follows

that the approach to prevention needs to be multifactorial. The landmark study conducted by Inouye in 1999,²⁹ and other prevention studies,^{30, 31, 32} have demonstrated that delirium can be prevented or at least moderated by addressing modifiable risk factors. This reflects a humanistic, compassionate approach to management based on high quality nursing and medical care (see Table 6).

Table 6: Delirium Prevention Strategies

Environmental Strategies	Clinical Practice Strategies
Orientation to time	Ensure function is optimised
<ul style="list-style-type: none"> • room with an unobstructed view to the outside world • lighting appropriate to the time of day • minimal lighting at night • provision of a clock and calendar suitable for an individual's vision 	<ul style="list-style-type: none"> • hearing aids • visual aids • regular mobilisation • encourage independence in activities of daily living • dentures and dental appliances well fitted and in place • encourage and assist if necessary to ensure adequate hydration and nutrition • monitor and regulate bowel function • promote relaxation and sufficient sleep

<p style="text-align: center;">Orientation to place</p> <ul style="list-style-type: none"> • avoid frequent room changes and keep room changes to a minimum • encourage family and carer's to bring in personal and familiar objects 	<p style="text-align: center;">Facilitate communication</p> <ul style="list-style-type: none"> • hearing aids • visual aids • interpreters and communication aids • dentures and dental appliances well fitted and in place
<p style="text-align: center;">Orientation to people</p> <ul style="list-style-type: none"> • encourage family and carer involvement by facilitating visiting • Orientate to personnel providing name and role 	<p style="text-align: center;">Ensure culturally sensitive approach</p> <ul style="list-style-type: none"> • awareness and respect of cultural and religious sensitivities
<p>Reduction in disturbance to environment</p> <ul style="list-style-type: none"> • single room to minimise disturbance of personnel attending to other patients at any time of the night and day • reduce incident noise especially, unpredictable sounds e.g. buzzers, alarmed medication delivery devices, televisions, trolleys • Reduce exposure to activity/stimulation e.g. Unavoidable disturbance if nursed in an acute environment where the likelihood of resuscitation, urgent intervention is likely • Facilitate undisturbed sleep at night • Avoid sleep deprivation 	<p style="text-align: center;">Maximise comfort</p> <ul style="list-style-type: none"> • Manage reduce discomfort and pain using nonpharmacological approaches when possible • minimise invasive procedures e.g. indwelling catheters; IV cannulas • address issues exacerbating emotional distress
<p style="text-align: center;">Provide routine</p> <ul style="list-style-type: none"> • scheduled rest period • encourage wakefulness during the day • Meal times at regular intervals and times • activities such as personal care at regular times 	<p style="text-align: center;">Minimise perception of threat</p> <ul style="list-style-type: none"> • avoid use of physical restraint • train personnel to use calm, confident manner keeping voice calm and even
	<p style="text-align: center;">Caution with medication</p> <ul style="list-style-type: none"> • review and minimise medication • avoid psychoactive drugs • avoid anticholinergic drugs • take careful drug and substance history and anticipate withdrawal syndromes from alcohol, nicotine, benzodiazepines, narcotics
	<p>Anticipate, prevent, identify and treat medically reversible problems</p> <ul style="list-style-type: none"> • screen high risk patients with a validated instrument e.g. CAM • thorough physical examination • dehydration • malnutrition • electrolyte abnormalities • hypoalbuminaemia • anaemia • renal impairment • urinary retention • depression

Secondary prevention requires optimal clinical management at the time of delirium and will be addressed below in the management section.

Tertiary prevention strategies require identification of previous episodes of delirium by taking a careful history to recognise high-risk individuals. A randomised placebo-controlled trial using low dose haloperidol in elderly hip-surgery patients at risk of delirium showed that although there was no difference in the incidence of delirium, the severity and duration of delirium, and length of hospital stay was reduced.³³

Investigation of the delirious patient

Delirium is generally at least partially reversible if the cause of the delirium can be identified and treated promptly. Investigation of a patient presenting with an acute confusional state should include the following elements:

- Thorough history including: alterations to sleep-wake cycle, nutrition, and recent misadventure including falls. It is essential to access corroborative history from carers, family, witnesses, access information including previous investigations from doctors involved in the care of the patient, allied health professionals, aged care assessment team members to establish the sequence of events, identify likely precipitating factors, the level of function and cognition prior to the presentation and if there have been any previous episodes of suspected delirium in the past.
- Review of medications including: medications taken prior to presentation, new medications commenced or medications ceased, adherence to treatment. In addition it is important to establish a substance use history including nicotine, ethanol, benzodiazepines, and other centrally acting drugs to identify risk of acute withdrawal.
- Thorough physical examination including: vital signs, postural blood pressure measurement, pulse oximetry, urine analysis, blood sugar level, palpation of the bladder for urinary retention and body weight. The physical examination may need to be targeted and opportunistic in the context of a patient exhibiting severe behavioural or emotional disturbance.
- Initially, investigations should be targeted at identifying or ruling out common causes of delirium in addition to investigations targeted at issues arising from history and examination. (Table 7) If the cause of delirium is not identified by this approach it may be necessary to conduct additional investigations aimed at identifying less common causes.

Table 7: Investigation of the delirious patient

Targeted blood tests:	Serum electrolytes including Ca Serum Creatinine Serum glucose Full blood count
Urine analysis	Mid-stream urine for microscopy, culture and sensitivity
Search for occult infection	Wound swab Sputum for microscopy, culture and sensitivity Consider blood cultures
Targeted investigations as informed by the history and investigation	Electrocardiogram Post void residual bladder scan Chest X-ray Head CT
Further investigations to be considered if no cause found by above approach	Thyroid function and thyroid antibody tests Drug levels Toxicology screen Vitamin B12 and folate levels Syphilis serology Lumbar puncture Electroencephalography Vasculitic screen including ANA and ENAs
ANA: Antinuclear Antibody; ENA: Extractable Nuclear Antibodies	

Current research is aimed at determining a biochemical marker for delirium. In a recent study C-reactive protein was found to be useful not only to predict incidence of delirium but also recovery from it. These results need to be interpreted with caution pending further investigation. C-reactive protein is well known to be a marker of inflammation, however it “*actually captures only one specific aspect of inflammation, which is not necessarily the most relevant for delirium and does not reflect all aspects of inflammation*”.³⁶

Management

Non-Pharmacological management of delirium

Non-pharmacological strategies similar to the interventions listed for prevention should be implemented whenever possible. Logically, if delirium is a multi-factorial problem, it follows that multidisciplinary interventions are likely to provide most success

in management. Bergmann et al,³⁷ have proposed a model of care for management of delirious patients in the acute setting with a standardised approach involving “four key steps: assessment of delirium symptoms in new admissions, evaluation and treatment of reversible causes of delirium, prevention and management of common complications of delirium, and restoration of cognitive and self-care function in delirious patients”. A randomised trial involving a multidisciplinary intervention encompassing: a standardised nursing intervention protocol, review by a geriatric specialist consultant and follow-up by an intervention nurse who liaised with all team members compared with usual care, conducted by Cole et al³⁸ failed to demonstrate that multidisciplinary care was more beneficial compared with usual care. A Cochrane Systematic Review is currently pending.³⁹ In the setting of delirium multicomponent intervention directed at prevention of delirium is likely to have much greater impact than stratagems aimed at treatment.⁴⁰

Pharmacological Management of Delirium

Administration of pharmacological agents should be reserved for patients with severe agitation or behavioural disturbance who are at risk of interrupting essential medical care and risk of causing harm to them self or others. This strategy outweighs risk associated with administration of the medication when symptoms cannot be controlled otherwise.²⁶

There are numerous guidelines available providing advice on approach to pharmacological management of delirium.^{2, 5, 11, 14, 21, 25, 26} Many institutions have developed their own protocols, procedures and guidelines adapted to local conditions.

Consensus opinion based on evidence from the literature supports the use of antipsychotics for the treatment of delirium. Traditionally low dose haloperidol has been considered the drug of choice as haloperidol is available in oral and parenteral dose forms, and has a lower incidence of adverse effects including anticholinergic side effects, postural hypotension, and sedation when compared with other traditional antipsychotic agents.²⁶ A recent Cochrane review conducted a literature review and meta-analysis “comparing the efficacy and incidence of adverse effects of haloperidol with risperidone, olanzapine and quetiapine in the treatment of delirium”.⁴¹ The authors concluded that there was no evidence that the atypical antipsychotics offered any advantage over low dose haloperidol. Higher doses of haloperidol (more than 4.5mg per day) were associated with an increased incidence of adverse reactions, mainly extrapyramidal side effects. The use of atypical antipsychotics remains controversial, as their administration has been associated with an increase in all cause mortality in the elderly population.⁴²⁻⁴⁶

In patients with co-existing medical conditions where use of dopamine antagonists are contraindicated, such as Lewy Body dementia and Parkinson's Disease, low doses of risperidone can be tried with careful monitoring.

Benzodiazepines are well recognised as appropriate treatment for alcohol or drug withdrawal. In practice, benzodiazepines with a short half-life and no active metabolites, for example, lorazepam, oxazepam, or midazolam may be of benefit for patients with excessive anxiety symptoms, with severe agitation not responding to anti-psychotics, or when antipsychotic medication is contraindicated.¹⁴ Benzodiazepine use can be associated with a worsening of confusion and sedation. A Cochrane Review pertaining to the use of benzodiazepines for delirium is pending.⁴⁷

Prognosis

Studies have shown that nearly half of patients with delirium are discharged from the acute hospital setting with persistent symptoms and of these, 20-40% still have delirium at 12 months.⁴⁸ Longer term outcomes in these patients are consistently worse than in those patients who fully recover by point of discharge, and it is unknown whether these patients will ever recover.

It is essential to use a multidisciplinary team approach to discharge to ensure adequate support for patients and their carers. Ideally, there should be close communication between the hospital team, primary care and the patients' family or caregivers. Education should be provided on what to expect with regards to the patient's function and prognosis. The patient should have regular review every few days in the community and minimum follow up should be 6 months.⁴⁸

Practical Key Points

- Every elderly patient admitted with confusion should be presumed to have delirium until proven otherwise.
- Improve early detection using the CAM and serial cognitive testing.
- Implement clinical guidelines, practice changes and education programmes for all medical, nursing and allied health staff.^{49, 50}
- Education and support of families and carers is essential
- Ensure close follow up in the community and good communication between hospital staff and primary care.

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