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PEER REVIEWED FEATURE
2 CPD POINTS

CLINICAL INVESTIGATIONS FROM THE RACP

Investigation of acute confusion in the elderly

SUZANNE WASS MB ChB, FRACP; **PENELOPE J. WEBSTER** MPH, MB BS, BPharm, FRACP; **BALAKRISHNAN (KICHU) R. NAIR** AM, MD, FRACP, FRCP

In this series, we present authoritative advice on the investigation of a common clinical problem, especially commissioned for family doctors and written by members of the Royal Australasian College of Physicians.

Key points

- **Presume that every elderly patient with confusion has delirium until proven otherwise.**
- **Early detection can be improved with the use of the Confusion Assessment Method and detailed history taking from family or carers.**
- **Formulate individual nonpharmacological management plans, and reserve antipsychotic or sedative medication for those with the most distressing symptoms.**
- **Education and support of families, carers and residential home staff is essential.**
- **Ensure close follow up in the community and good communication between carers and primary care practitioners.**

Delirium is a common syndrome affecting many elderly patients in both hospital and community settings. It is complex and often multifactorial and therefore continues to be underdiagnosed and consequently poorly managed. With the increasing burden of an ageing population, delirium remains a major challenge for all healthcare workers.

DEFINITION

The *Diagnostic and Statistical Manual of Mental Disorders V* (*DSM-V*) defines delirium as: 'a disturbance in attention (i.e. reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment ... [that] develops over a short period of time (usually hours to a few days), that represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.'[1]

Delirium should be suspected in any elderly patient presenting with an acute change in cognition, reduction in clarity of awareness, inability to focus or distractibility. Delirium can be clinically divided into three categories:

- hyperactive – characterised by periods of agitation, aggression or wandering
- hypoactive – patients are often quiet and withdrawn
- more commonly, a fluctuation between the two.[2-5]

Dr Wass is a Staff Specialist Geriatrician and General Physician at the Calvary Mater Hospital, Newcastle.
Dr Webster is a Staff Specialist in Geriatric Medicine at the Hunter New England Area Health Service.
Professor Nair is a Professor of Medicine and Associate Dean of Continuing Medical Professional Development in the School of Medicine and Public Health, University of Newcastle, Newcastle, NSW.
SERIES EDITOR: Christopher S. Pokorny MB BS, FRACP, FRCP, FACG
Associate Professor Pokorny is Conjoint Associate Professor of Medicine, University of New South Wales, and Visiting Gastroenterologist, Sydney and Liverpool Hospitals, Sydney, NSW.

1. CLINICAL FEATURES OF DELIRIUM

Essential features

- Acute onset
- Fluctuating severity during the course of a day
- Disturbance in attention
- Disturbance in cognition
- Not better explained by another neurocognitive disorder
- Does not occur in the context of a severely reduced level of consciousness, such as a coma

Variable features

- Perceptual disturbance
- Hyper- or hypoactive
- Altered sleep/wake cycle
- Emotional disturbance
- Agitation or aggression

Adapted from Inouye SK. Delirium in older persons. N Engl J Med 2006; 354: 1157-1165.[20]

2. COMMON RISK FACTORS FOR DELIRIUM

Noncorrectable

- Age
- Male sex
- Mild cognitive impairment, dementia or Parkinson's disease[19]
- Multiple comorbidities including:
  - renal and hepatic disease
  - history of cerebrovascular accident
  - history of falls and poor mobility
  - history of prior delirium

Correctable

- Hearing impairment or visual impairment (associated with a threefold increased risk[21])
- Malnutrition, dehydration or low albumin (associated with a twofold increased risk[21])
- Social isolation, sleep deprivation, new environment, recent move into a residential aged care facility[22]
- Restraints and indwelling catheters
- New medication or three or more medications
- Any medication with anticholinergic properties
- No time orientation
- Smoking

Potentially correctable

- Uraemia; blood urea of more than 10 mmol/L is an independent risk factor[23]
- Depression
- Prolonged hospital stay, increased risk after nine days[5]

OCCURRENCE AND CONSEQUENCES OF DELIRIUM

Of all elderly patients in hospital, 15 to 30% will have delirium on admission and up to 56% will develop delirium during their stay.[6] The point prevalence of delirium in the community is 1.1% among those aged over 55 years and 14% in those over 85 years.[7] The incidence among nursing home residents surpasses 60%.[1]

It is estimated that delirium incurs direct healthcare costs of $150 billion each year in the USA; the actual cost of delirium in Australia has not been published.[8] This figure does not include additional costs in the form of increased residential care, rehabilitation and home services associated with delirium.[9,10]

The cost to the patient is also high because delirium can lead to significant mortality and morbidity, including:

- prolonged hospital stay (on average eight days longer than for those without delirium)[3]
- 40% mortality at one year[1,11-14]
- increased risk of developing complications such as hospital-acquired infections, pressure ulcers, incontinence and falls (despite the use of restraints)[4,15]
- poor physical and cognitive recovery at six and 12 months,[15] with lower scores on the Mini Mental State Examination (MMSE) at discharge compared with control patients[16]
- increased risk of placement in a residential home[1,13,14]
- increased risk of developing dementia even in patients with no cognitive impairment at baseline.[17,14]

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

PATHOPHYSIOLOGY

In recent years, there has been significant research aimed at untangling the pathophysiology underlying delirium and its consequences in an attempt to allow more targeted prevention and management strategies. Not surprisingly, much of this research has been performed in the intensive care setting which has the highest prevalence of patients with delirium.[18]

There are several hypotheses concerning the pathophysiology of delirium including an imbalance in dopaminergic, cholinergic and/or serotonergic neurotransmitter systems; endothelial dysfunction; reduction in brain perfusion; and deterioration in the effectiveness of the blood–brain barrier increasing the exposure of the brain to potentially toxic pathogens. Another view is that delirium could be a consequence of a systemic inflammatory response leading to increased levels of proinflammatory cytokines that cause injury to the brain and brain dysfunction.[19]

CLINICAL FEATURES

Clinical features that can be associated with delirium are described in Box 1.[20] Delirium can be preceded by a period of prodromal illness, usually hours to a few days, where the patient may appear impatient, anxious, restless, distracted and develop urinary incontinence. They may refuse investigations. In hindsight, family members are able to give a history of this prodromal period but it is difficult to detect clinically.[21] Elderly patients with delirium often present with behavioural changes first, which may be the only indication of underlying medical illness.

Lewy body dementia has a rapid onset, the confusion often fluctuates and patients have vivid visual hallucinations. This makes Lewy body dementia an important differential diagnosis to consider when a person presents with suspected delirium.

RISK AND PRECIPITATING FACTORS

Most elderly patients have multiple risk factors, making them more susceptible to delirium (see Box 2). Precipitating factors include prescribed medication and polypharmacy or alcohol and benzodiazepine withdrawal (a full list is given in Box 3). Attention to all possible risk and precipitating factors, and modification if possible, will ensure the best outcome for the patient.

RECOGNISING PATIENTS WITH DELIRIUM

Elderly patients with an acute decline in cognition should be presumed to have delirium until proven otherwise. Studies show that 30 to 67% of patients with delirium go undetected,[5,22] which is why a corroborative history from family or carers is essential to establish the acute decline in cognition, in addition to cognitive screening. The Australian and New Zealand Society for Geriatric Medicine (ANZSGM), the American Psychiatric Association and the British Geriatrics Society all recommend the Confusion Assessment Method (CAM), a

3. COMMON PRECIPITATING FACTORS

- Prescribed medication and polypharmacy
- Alcohol and benzodiazepine withdrawal
- Sepsis, shock, hypothermia
- Electrolyte disturbance (sodium, calcium, magnesium, phosphate)
- Endocrine disturbance (blood sugar, thyroid)
- Nutritional deficiencies (thiamine, vitamin B_{12}, folate)
- Cardiac, liver or renal failure
- Pulmonary disorders (particularly in the setting of hypoxaemia)
- Cerebrovascular accident or seizures
- Postsurgery, especially cardiac, orthopaedic or with intensive care unit stay
- Falls and fractures
- Anaemia or gastrointestinal bleed
- Pain
- Cancer and terminal illness

4. CONFUSION ASSESSMENT METHOD (CAM)

1. Acute onset and fluctuating course

- Is there evidence of change in cognition from baseline?
- Does this fluctuate during the day?

2. Inattention

- Dose the patient have difficulty focusing attention?
- Do they seem distracted?

3. Disorganised thinking

- Does the patient have disorganised thinking, rambling speech or seem incoherent?

4. Altered level of consciousness

- Would you describe the patient as being hyperalert, lethargic or drowsy, or in a stupor or coma?

A diagnosis of delirium requires a yes answer to questions 1 and 2 and either 3 or 4.

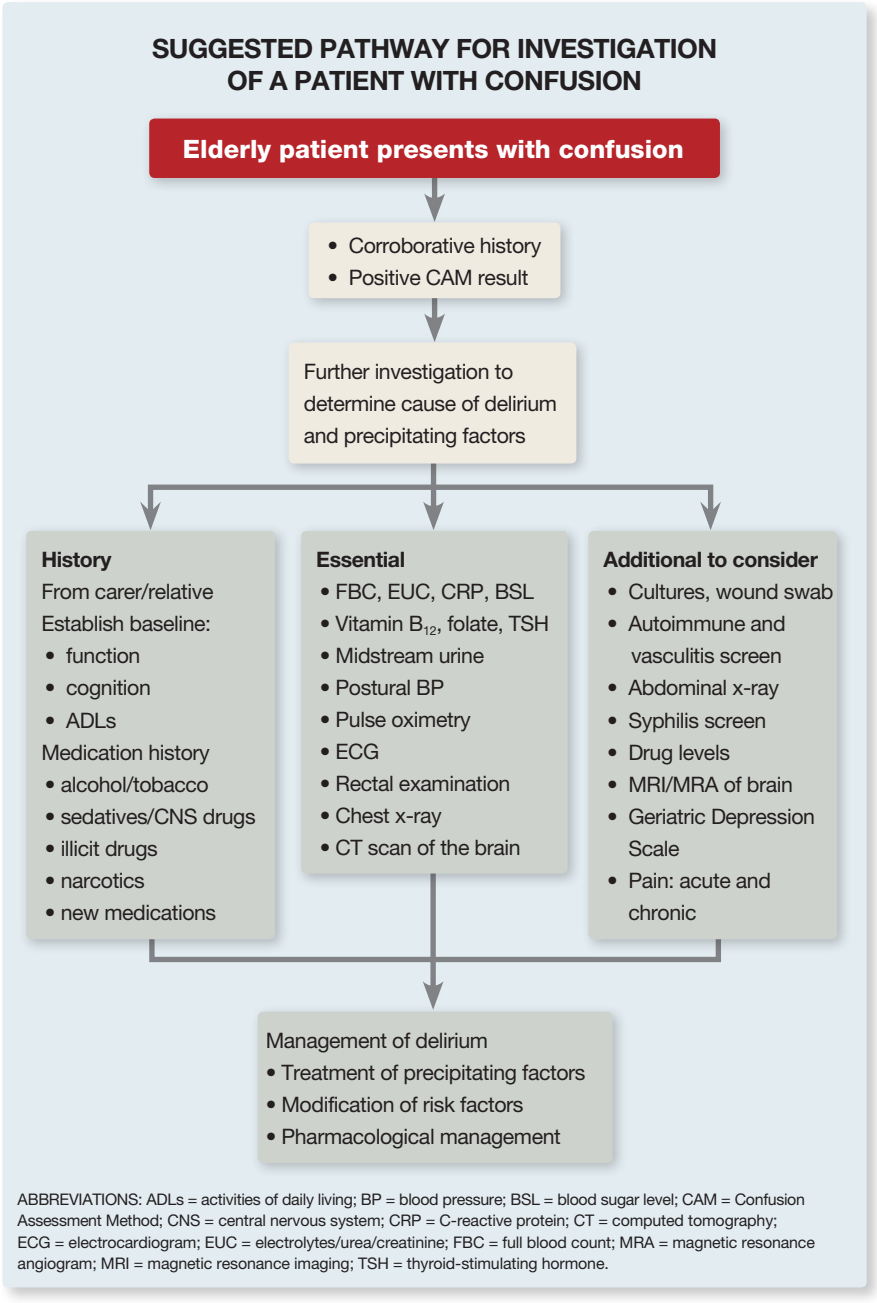
Note: Exclude Lewy body dementia.

Adapted from *Harrison's Online*, Chapter 26. Confusion and delirium, McGraw-Hill Companies.[2]

TABLE. 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	Hallucinations, delusions rare except in Lewy body dementia	Can have complex delusions, paranoid psychosis
MMSE	Distracted, difficulty completing MMSE	Struggles; tries to find correct reply	Lacks motivation; 'I don't know'

ABBREVIATIONS: MMSE = Mini Mental State Examination. Adapted from Milisen K et al. Nurs Clin Nat Am 2006; 41: 1-22.[25]



ABBREVIATIONS: ADLs = activities of daily living; BP = blood pressure; BSL = blood sugar level; CAM = Confusion Assessment Method; CNS = central nervous system; CRP = C-reactive protein; CT = computed tomography; ECG = electrocardiogram; EUC = electrolytes/urea/creatinine; FBC = full blood count; MRA = magnetic resonance angiogram; MRI = magnetic resonance imaging; TSH = thyroid-stimulating hormone.

screening tool specifically designed to detect delirium (see Box 4). This has a reported sensitivity of more than 94% and a specificity of more than 90% and is easy to use in a clinical setting.[4,23]

The MMSE is often used to test cognitive function and although it is used in the setting of delirium, it was not designed for this purpose. To use the MMSE in patients with delirium, it is necessary to know baseline scores and engage the patient in repeat testing throughout their illness, which may be effective but is also time-consuming.

It can be difficult to differentiate between delirium, dementia and depression in clinical practice. About 42% of inpatients referred to psychiatric services for depression actually have delirium.[24] The Table summarises the main differences; however, even in patients diagnosed with dementia or depression, any new changes in cognition must be investigated as delirium.[25]

INVESTIGATION

Delirium may be reversible if the causes can be identified and treated promptly. Investigation of a patient presenting with an acute confusional state is summarised in the Flowchart on this page. There is no evidence to support a specific chemical biomarker to detect delirium.[26]

MANAGEMENT

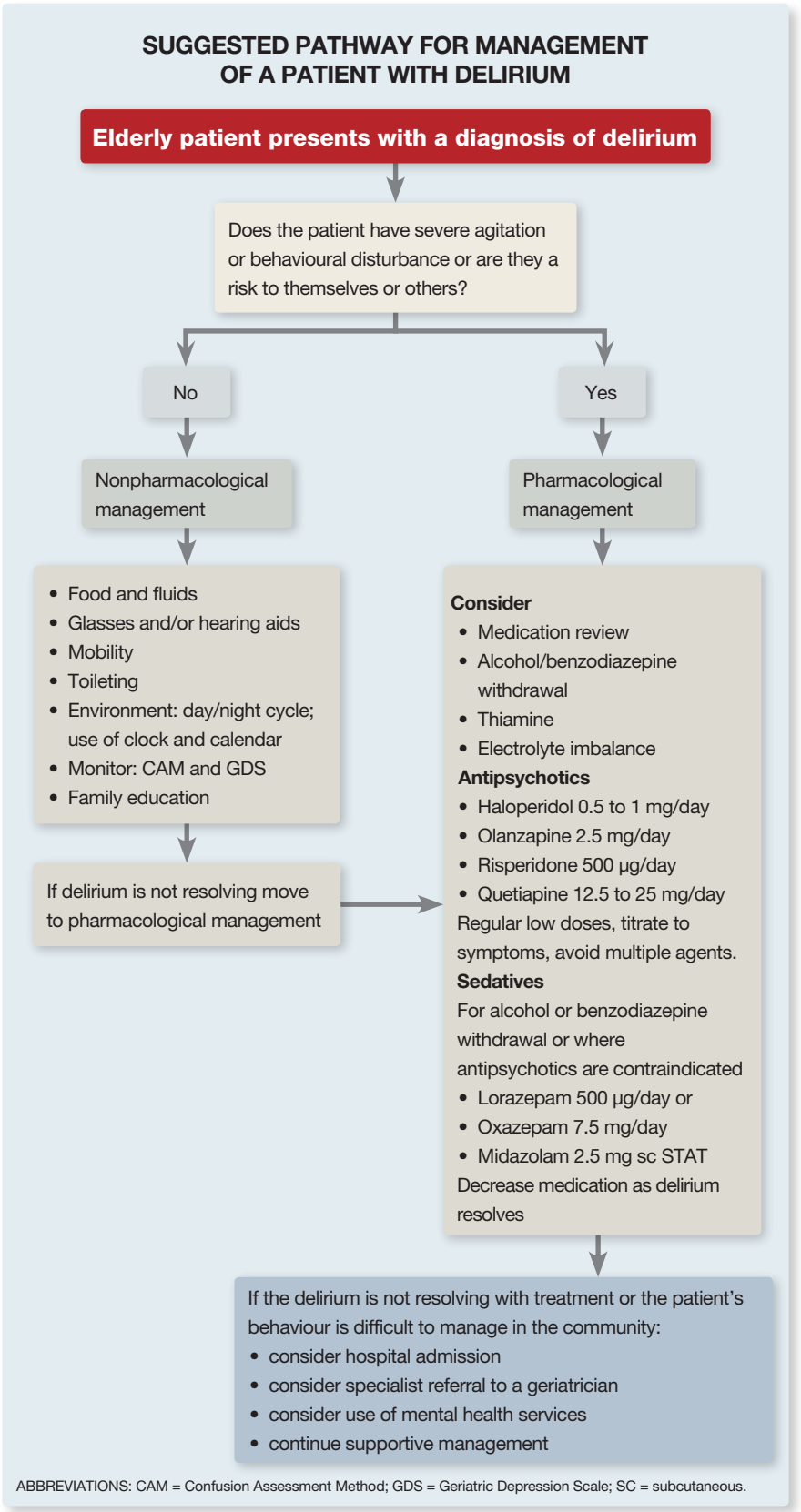
Nonpharmacological management

Nonpharmacological strategies are particularly useful for patients in hospitals or residential homes. The plan should be tailored to the individual and, whenever possible, implemented before the use of antipsychotic or sedative medications (see the Flowchart on page 46). It should be highlighted that pharmacological intervention should be the last resort and often is associated with side effects.

Delirium is a multifactorial problem and it follows that multidisciplinary interventions are likely to be successful. However, clinical trials have failed to show significant results in terms of reducing the duration of delirium, length of inpatient stay or healthcare costs.[27,28] Two Cochrane reviews on delirium in hospitalised patients and residential home residents are available.[29,30] Multicomponent intervention directed at the prevention of delirium is likely to have a much greater impact than strategies aimed at treatment.[31] Moreover, this has been shown to have a positive effect on staff attitudes and patient care.[32]

Pharmacological management

Administration of pharmacological agents should be reserved for patients with severe agitation or behavioural disturbance resulting in risk to themselves or others or severe patient distress that outweighs the risks associated with sedative and antipsychotic medications. No specific agent is licensed for use in patients with delirium and there is no evidence that specific therapeutics have an effect on the duration or severity of delirium. Utmost caution should be exercised when prescribing antipsychotic medication to patients with a diagnosis of Lewy body



dementia because they exhibit increased sensitivity to these drugs and this condition can mimic delirium as mentioned earlier. Adverse reactions include Parkinsonian side effects such as rigidity, immobility, reduction in function and ability to communicate. There has been an association with sudden death in some studies.

Antipsychotics are the most common class of drug prescribed for patients with delirium, and traditionally haloperidol has been the agent of choice.[33] However, haloperidol has poor sedative properties, and the doses required to improve severe agitation are associated with increased risk of anticholinergic and extrapyramidal side effects.[34] More recent evidence supports the use of atypical antipsychotics such as olanzapine, risperidone and quetiapine (all used off label), which appear to have equal efficacy when compared with haloperidol. They also appear to be better tolerated in the elderly population and allow for flexible dosing regimens with lower side effects.[35-38] There is some emerging evidence that quetiapine may decrease the severity of delirium symptoms, but studies are small and more research is needed.[39,40] At present, there is no evidence to support the use of cholinesterase inhibitors in the treatment (or prevention) of delirium.[41-43]

Benzodiazepines are an appropriate treatment for patients with alcohol or drug withdrawal, or when antipsychotic medication is contraindicated (i.e. in patients with Lewy body dementia or Parkinson's disease).[4,44] Benzodiazepines with a short half-life and no active metabolites, such as lorazepam, oxazepam or midazolam, are preferred (all used off label). Benzodiazepines can be associated with a worsening of confusion and sedation and should be used with caution.

Whichever agent is chosen, frail elderly delirious patients will be at increased risk of adverse events associated with antipsychotic and sedative medication, and longer-term use is associated with an increase in all-cause mortality.[45-49] General principles for use are as follows:

- reserve medication for severe agitation causing distress or putting the patient, staff or other patients at risk
- start at a regular low dose and titrate if necessary
- avoid multiple agents
- use in a supervised environment, such as a residential home or with carer supervision
- reduce and stop the medication

once the symptoms of delirium have improved.

Despite early detection and best management, some patients will require hospital admission to further investigate delirium and manage behaviours. Consider early referral to specialist services such as the Community Geriatrician, mental health services for older people, the Dementia Behaviour Management Advisory Service (http://dbmas.org.au/) or community service package providers. Studies have shown that almost half of patients with delirium are discharged from the acute hospital setting with persistent symptoms and, of these, 20 to 40% still have delirium at 12 months. There should be close communication between primary care practitioners and the family or carers to provide education and ongoing support. Further assessment and monitoring of cognitive function may be required, and the minimum follow up for cognitive assessment should be six months.[50]

CONCLUSION

Acute delirium is very common in the elderly and is associated with significant morbidity and mortality. It is often underdiagnosed and places a significant burden on patients, families and the healthcare system. With Australia's changing demography, every doctor should be well equipped to manage delirium. Delirium is an important diagnosis to make and manage. MT

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A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

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SUZANNE WASS MB ChB, FRACP; **PENELOPE J. WEBSTER** MPH, MB BS, BPharm, FRACP;
BALAKRISHNAN (KICHU) R. NAIR AM, MD, FRACP, FRCP

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