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Delirium in the Elderly
Optimal Management

Jonathan M. Flacker and *Edward R. Marcantonio*

Department of Medicine and the Research and Training Institute, Hebrew Rehabilitation Center for Aged, and the Division on Aging, Harvard Medical School, Boston, Massachusetts, USA

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Abstract

Delirium is common, morbid and costly, especially among hospitalised elderly patients. Nonetheless, it remains under-recognised and often poorly managed. This article summarises the 5 key steps in the optimal management of delirium.

The first step is to precisely define the syndrome of delirium, using key features described in the Diagnostic and Statistical Manual of Mental Disorders (fourth edition) [DSM-IV] or the Confusion Assessment Method. Key features include an acute onset of mental status change, fluctuating course, the presence of inattention, and either disorganised thinking or an altered level of consciousness.

The second step involves the identification of patients at high risk of delirium before it develops, so that preventive measures can be implemented. Risk factors for delirium include advanced age, dementia, impaired functional status, chronic comorbidities and medications, and the severity of the acute illness or surgery.

The third step is improved recognition of delirium. Very often, the presence of delirium is neither diagnosed nor properly documented in the medical record. The fourth step is to appropriately evaluate the delirious patient to assess all important contributors to the syndrome. This evaluation will usually involve a careful history, medication review, physical examination and selected laboratory testing.

The fifth, and most important, step is the management of the delirious patient. The key elements of management are treating the primary condition(s) leading to delirium, removing all treatable contributing factors, maintaining behavioural control, and supporting the patient and their family.

Delirium is a common complication of illness, particularly in the elderly. Approximately 10% of elderly patients may be delirious on presentation to hospital,[1,2] and the prevalence of delirium is estimated to be 15 to 38% of elderly medical inpatients.[3-7] The incidence of delirium following surgery depends on the specific procedure, but it may exceed 50% in some populations such as those undergoing hip fracture repair.[8] Delirium has significant human and economic burdens; for example, increased morbidity, prolonged hospitalisation and subsequent functional decline.[9]

Delirium may occur in people of any age, although elderly people appear to be at especially high risk. Furthermore, several aetiologies of delirium with specific pathophysiologies and treatments have been identified. These include alcohol (ethanol) withdrawal, resulting in delirium tremens and hepatic encephalopathy. Unfortunately, in most cases, the neuropathophysiology of delirium is not clear. This article does not focus on the management of conditions with a specific pathophysiology and treatment, but instead addresses a general approach to the management of elderly patients with acute delirium from unclear, illness-related or multifactorial causes.

1. Definition

The terminology surrounding delirium has often added to the confusion about this syndrome. The commonly used term 'acute confusional state' is rather apt, but other terms, ranging from 'organic brain syndrome' to 'subacute befuddlement', are not well defined[10] and are at times misleading. To address this problem, several diagnostic and evaluative instruments for delirium have been developed.[11]

The criteria for delirium attributable to a general medical condition,[12] as described by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), are listed in table I. DSM-IV is commonly used and provides a useful starting point for understanding the diagnosis of delirium. Several key features of delirium are cited, including disturbance of consciousness and acute onset with fluctuation, which typify this syndrome. Another DSM-IV criterion is a change in cognition that is not better accounted for by a pre-existing, established or evolving dementia. DSM-IV describes other subcategories of delirium, including substance-induced delirium, substance withdrawal delirium, delirium attributable to multiple aetiologies, and delirium not otherwise specified.

Table I. DSM-IV diagnostic criteria for delirium[12]

Disturbance of consciousness (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention
A change in cognition (e.g. memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia
The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day
There is evidence from the history, physical examination or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition

The DSM-IV definition provides a framework for research into delirium, but this can be difficult for the clinician to apply. One reason for this is that delirium and dementia often coexist, and the DSM-IV criteria are not particularly helpful in making the important clinical decision as to whether the patient's mental status change is attributable to delirium, dementia or both. In addition, the DSM-IV diagnostic criteria represent expert opinions that have not been prospectively tested and validated. Furthermore, the criteria change every few years; thus, comparison between studies performed several years apart can be difficult, since different versions of the DSM may identify different populations as having delirium.[13] Finally, most of the described delirium subcategories do not alter the general approach to the care of such patients, and the diagnostic category to which the patient should be assigned is often not clear until after complete or partial resolution of the syndrome.

Many other instruments for the assessment of delirium have been developed. Instruments measuring the severity of delirium include the Delirium Rating Scale,[14] the Memorial Delirium Assessment Instrument[15] and the Confusional State

Evaluation.[16] In addition, the Delirium Symptom Interview[17] assesses the presence of several major symptoms of delirium, but is neither a diagnostic instrument nor a severity scale *per se*.

One of the most useful delirium assessment instruments for the general clinician is the Confusion Assessment Method (CAM) (table II).[18] The CAM was adapted from the DSM-IIIR[19] criteria for delirium to 'enable non–psychiatrically trained clinicians to identify delirium quickly and accurately in both clinical and research settings'. The CAM has been validated against expert psychiatric ratings and is both sensitive (94 to 100%) and specific (90 to 95%).[18] The CAM has also proven to be useful for research on delirium.[2,6,20,21]

Five features are assessed using the CAM: (i) acute onset of symptoms; (ii) fluctuating course; (iii) inattention; (iv) disorganised thinking; and (v) altered consciousness. To diagnose delirium, the first 3 symptoms must be present, along with either of the last two. This method focuses on the essential features of the syndrome rather than its cause, and avoids the diagnostic problems inherent in the DSM-IV criteria.

To elaborate, delirium always involves an acute change in mental status. This is in contrast to the insidious deterioration of mental status that is seen in progressive dementia (e.g. Alzheimer's disease). Thus, knowledge of the patient's baseline mental status is a key element in the diagnosis of delirium. Ideally, a baseline mental status test will be documented using a short, validated instrument such as the Mini-Mental State Exam.[22] Unfortunately, this rarely occurs in clinical practice. The clinician usually has to rely on the reports of family members or other caregivers regarding recent mental and physical functional changes. Statements such as the patient 'is not him/herself', 'has lost his/her memory', or 'is acting strangely' should be heeded as potentially important clues. In addition, since pre-existing dementia does not rule out superimposed delirium, the severity of the underlying dementia and changes from baseline should be ascertained from those who know the patient well.

Table II. The Confusion Assessment Method (CAM).[18] The diagnosis of delirium requires the presence of features 1, 2 and 3, and either 4 or 5

1. Acute change in mental status *Is there evidence of an acute change in cognition from the patient's baseline?*
2. Fluctuating symptoms *Does the abnormal behaviour fluctuate during the day (i.e. tends to come and go, or increase and decrease in severity)?*
3. Inattention *Does the patient have difficulty focusing attention (e.g. the patient is easily distracted, or is having difficulty keeping track of what is being said)?*
4. Disorganised thinking *Is the patient's thinking disorganised or incoherent (e.g. the patient is rambling or has irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject)?*
5. Altered level of consciousness *Is the patient's mental status anything besides alert [i.e. vigilant (hyperalert), lethargic (drowsy, easily aroused), stuporous (difficult to arouse) or comatose (impossible to arouse)]?*

Delirium always fluctuates. The fluctuations can occur over minutes to hours, and although the patient may at times appear 'normal', subtle abnormalities can usually be detected. Again, the astute clinician heeds clues from caregivers and family members such as 'he was fine a few minutes ago' or 'sometimes we can't wake him, other times he's a wild man'.

A very important diagnostic feature of delirium is the presence of abnormal attention. Inattention in this sense does not refer to a focal neurological finding such as hemispatial neglect, but rather a global failure to focus motivation and perform cogent and sustained tasks. Attention can be tested formally by forward digit span (normally up to 7 digits forward can be repeated) or trail-making tests. Backward digit span and reciting the months of the year backwards also require attention, but these tasks require more complicated mental manipulation. Less formally, inattention is often obvious after trying to take the patient's history, either because of an inability to shift attention (leading to perseveration), an inability to focus attention (leading the examiner to repeat questions) or hyperattentiveness (leading to response to distracting stimuli such as questions posed to a room-

mate). Often, the 'poor historian' is actually delirious, especially if a normal baseline mental status has been documented.

An altered level of consciousness may mean that delirium is present. Delirium has been categorised into four variants according to the level of consciousness:

- hyperactive
- hypoactive
- mixed
- normal.

In one study of 125 delirious hospitalised elderly patients,[23] the hyperactive variant was present in 15%. Hyperactive delirium tends to be the easiest to recognise because patients are usually loud, rambunctious and disruptive, and if this behaviour is not noted by the physician it will usually be noticed by the nurse.

Hypoactive delirium, which was present in 19% of patients in the aforementioned study,[23] is more subtle and is often missed. People with hypoactive delirium may be considered 'good patients'. They will sit quietly in their bed, often not eating or drinking, until someone takes note of the mental status abnormality.

The largest group of patients is those with 'mixed delirium' (i.e. having features of both hyperactive and hypoactive delirium), who comprised 52% of the population in the study by Liptzin and Levkoff.[23]

Because the symptoms of delirium fluctuate, it is possible to have an apparently normal level of consciousness and still be delirious. This was the case in 14% of those in the study cited above.[23] Such patients meet CAM criteria for delirium because they display disorganised thinking. Disorganised thinking is characterised by rambling and illogical conversation. Such patients may jump unpredictably from one subject to another and are unable to focus their attention despite appearing, superficially, to be alert. Most patients with delirium will exhibit both disorganised thinking and an altered level of consciousness.

Some commonly observed behaviours are not included in the CAM because their presence is not diagnostic for delirium. These include abnormal psychomotor activity, sleep-wake cycle alterations, hallucinations, delusions, abnormal speech patterns, tremor and emotional lability. Any or all of these behaviours may be found in delirious individuals, and their onset should prompt evaluation.

2. Prevention

The optimal approach to the management of delirium is to prevent its occurrence in the first place. An important initial step is to identify those most at risk. It is generally believed that the risk of delirium is a composite of the patient's pre-existing vulnerabilities and the severity of the precipitating insult or illness. That is, the less vulnerable the patient, the worse the insult must be to produce delirium. The corollary is also true: very vulnerable patients may become delirious after seemingly minor insults.

One recent study[24] graphically demonstrated the validity of this model. In this study, vulnerability was defined by a previously validated model that included visual impairment, illness severity, cognitive impairment and a serum urea nitrogen : creatinine ratio of ≥18. The severity of insult was measured by the presence of malnutrition, use of physical restraints, greater than 3 medications added, use of a bladder catheter or any iatrogenic event. In 125 patients with low vulnerability scores and few insults, the incidence of delirium was 0% per day; in 69 individuals with the highest vulnerability and the most insults, the delirium incidence was 11.6% per day.

According to the above reasoning, a fairly clear portrait of the person at greatest risk for delirium can be drawn. Older individuals with dementia and multiple chronic illnesses, particularly those undergoing surgery, may require only a mild infection and/or change of environment (such as the hospital or subacute care unit) to precipitate delirium. Younger, cognitively intact patients typically require much more severe stressors, such as a postsurgical state, sleep deprivation, hypoxia and psychoactive medications, to precipitate delirium.

Table III. Drugs associated with delirium

Hypnosedatives	Benzodiazepines, especially long-acting drugs (e.g. diazepam, flurazepam, chlordiazepoxide) Short-acting drugs are less problematic, except triazolam and alprazolam Delirium may occur either with initiation or withdrawal Barbiturates (severe withdrawal syndrome) Chloral hydrate and others Alcohol (ethanol)
Antidepressants	Especially tertiary amines (e.g. amitriptyline, imipramine, doxepin), which are highly anticholinergic Selective serotonin (5-hydroxytryptamine; 5-HT) reuptake inhibitors (less commonly)
Anticholinergics	Diphenhydramine, oxybutynin, benzatropine (benztropine)
Opioid analgesics	Any, but especially pethidine (meperidine), which is highly anticholinergic
Antipsychotics	Uncommon, but low potency, highly anticholinergic agents more likely Atypical antipsychotics (including clozapine)
Anticonvulsants	Especially phenytoin at high serum concentrations
Histamine H_2 receptor antagonists	
Antiparkinsonian agents	Amantadine Levodopa-carbidopa Dopamine agonists (e.g. pergolide, bromocriptine)

A comprehensive list of all the proposed risk factors and precipitants of delirium would be unmanageably long. Rather, the important point is that minimising the physiological and psychological stressors on patients also minimises the risk of delirium. Such stressors may be premorbid patient characteristics (e.g. dementia, depression, alcohol use) or illness-related factors (electrolyte imbalance, anaemia, hypoxia, constipation). As a general rule, anything that can be corrected should be corrected, unless the risks and burdens of such treatments outweigh their potential benefits.

Furthermore, medical care should be proactive, and potential problems should be anticipated before they occur. For example, gentle overnight hydration of an elderly person undergoing an overnight bowel cleansing preparation may prevent subsequent delirium caused by dehydration.

Medication use is one of the most important modifiable factors that can cause delirium. A list of the medications that are most commonly associated with delirium are listed in table III. Antipsychotic medications such as haloperidol block dopamine receptors in the brain, and their use has been associated with delirium in medical inpatients.[25] Whether the antipsychotic drug was a cause or consequence of delirium is unclear because of the cross-sectional nature of this study. In a similar fashion, both opioid analgesics and benzodiazepines have been associated with delirium in some[5] but not all[7,25] epidemiological studies.

Other common medications that have been reported to precipitate delirium include histamine H_2 receptor antagonists,[26] digoxin,[27] ciprofloxacin[28] and fluoxetine.[29]

Anticholinergic medications deserve special attention. Ample evidence exists implicating anticholinergic drugs and toxins as a cause of delirium.[30,31] Furthermore, an animal model of delirium can be created by treating rats with the anticholinergic agent atropine.[32] Curiously, 'anticholinergic medications' have not been consistently associated with delirium in epidemiological studies of medical inpatients,[5,24] perhaps because of insufficient statistical power or because individual susceptibilities to the effects of such medications vary greatly. However, most opioid analgesics [particularly pethidine (meperidine)] are known to produce delirium,[33] and many other medications not generally thought of as anticholinergics block central muscarinic receptors *in vitro*.[34] Thus, the lack of association between delirium and anticholinergic medications in epidemiological studies is probably one of misclassification of drug effects rather than the inability of the anticholinergic effects of drugs to produce delirium. In fact, the level of measured anticholinergic substances in the blood (using a radionuclide dis-

placement assay) is a strong independent predictor of delirium in elderly medical patients.[21,35]

In surgical patients, the situation is similar. The use of opioids or benzodiazepines is associated with the occurrence of delirium.[36] Anticholinergic drug use has been associated with delirium in orthopaedic patients,[37,38] but another study of patients undergoing general, orthopaedic or gynaecological surgery[36] found no such association. In surgical patients, serum anticholinergic activity has been associated with delirium in small uncontrolled studies.[39,40] Significantly, the type of anaesthesia does not seem to be important, with similar rates of postoperative delirium among those treated with spinal epidural and general anaesthesia.[41,42] However, one randomised study of 57 elderly patients with femoral neck fracture[43] found that common complications of the type of anaesthesia chosen, such as hypoxaemia with general anaesthesia and hypotension with spinal anaesthesia, may play an important role in the development of delirium.

It is important to note that the withdrawal of medications and drugs of abuse, such as alcohol, may cause delirium. Alcoholism and chronic benzodiazepine use are unfortunately quite common in older persons. If these dependencies are unrecognised, hospitalisation may lead to inadvertent withdrawal and delirium. Such withdrawal syndromes may be especially important in elderly individuals whose mortality from delirium tremens may be up to 27%.[44] Delirium following clozapine withdrawal has been reported, possibly caused by central cholinergic rebound following discontinuation of the medication.[45] Obtaining a thorough history from the patient and their caregivers is crucial to the prevention of withdrawal delirium.

Several studies suggest that prevention of delirium is possible, at least for some surgical patients.[46] Although these studies have had important methodological limitations, including the failure to adequately blind investigators or randomise patients, they have demonstrated that prevention measures are modestly effective. The best of such studies include 2 carried out in elderly orthopaedic patients. The first, by Williams et al.,[47] used a broad range of interventions to treat pain, sensory impairment, immobility, disorientation attributable to a new environment, loss of independence, evening confusion and pain. In the second study (n = 214), Gustafson et al.[48] found a 14% absolute risk reduction in the occurrence of delirium by providing geriatric consultation, subcutaneous low dose heparin, supplemental oxygen, morphine for pain control, and treatment of hypotension and heart failure. The impact of other interventions, such as providing calendars and clocks to all patients for orientation purposes, assuring that eye-glasses and hearing aids are provided when needed, calm reorientation, touch and reassurance, is not known. However, these measures are low-cost, nontoxic and seem eminently worthwhile.

In summary, we suggest the following principles to prevent delirium. First, it is possible to identify high risk individuals who, in general, are the more frail elderly. Secondly, many of the important precipitants can be prevented by good medical care with attention to nutrition, hydration, medication use, bowel and bladder function, and the avoidance of iatrogenic complications. Thirdly, a brief screen to determine the patient's baseline mental status should be routinely performed in older persons, so that changes can be more easily recognised.

3. Recognition

Unfortunately, even when all preventive measures are taken, delirium may still occur. Many patients will already be delirious by the time they are evaluated by a healthcare provider. Unexplained delirium is a medical emergency and requires immediate investigation. Delirium may be the first sign of acute illness in some patients, preceding the development of more common disease indicators such as fever. In some cases, delirium may be the only clinical indication that something is wrong. It is therefore imperative to recognise the presence of delirium.

Unfortunately, several studies demonstrate that this does not always occur. A study of 250 elderly emergency room patients[49] found that 10% met

CAM criteria for delirium. A note reflecting the recognition of a change in mental status was made in only 13% of the delirious individuals. Furthermore, 29% of those with delirium were discharged home, about half of whom experienced subsequent problems following discharge. This finding was replicated in another study[2] where 17% of the patients who were screened and found to have delirium were subsequently discharged.

The recognition of delirium in medical and surgical inpatients is no better. In one prospective study of 111 patients with femoral neck fracture,[50] 68 (61.3%) were found by the investigators to have a postoperative acute confusional state (DSM-III criteria). However, the presence of acute confusional state was documented in the medical record by a nurse in 42 (37.8%) cases, and by a physician in only 9 (8.1%) cases. In a separate prospective analysis of 57 patients without dementia, acute confusional state was found in 25 (43.9%) patients postoperatively, but only documented in the medical record by a nurse in 17 (29.8%) cases, and by a physician in 4 (7.0%) cases. In another study of 133 consecutive patients admitted to the medical service of a tertiary care hospital,[51] delirium (DSM-III criteria) was found in 20 (15%) patients, yet only 1 case of delirium was diagnosed by the primary physician. Thus, it seems clear that the failure to diagnose delirium is an important barrier to the proper management of this syndrome.

4. Evaluation

Making the diagnosis of delirium is only the end of the beginning. The most important part of the delirium workup is not its diagnosis, but rather the search for and correction of potentially contributing aetiological factors. Several important principles guide this search. Although delirium is a neurological condition, the major factors responsible are typically found outside the CNS. In addition, the search for precipitants should not stop once one factor has been identified; most hospitalised elderly patients have several important contributors to delirium, and optimal management requires attention to each. Therefore, a thorough history, physical examination and medication review is imperative.

Medications are perhaps the most common modifiable causes of delirium. All delirious patients deserve a careful review of their medications with particular attention to recent additions, changes in dosage and discontinuations (for withdrawal delirium). Medications used on an 'as required' basis must not be overlooked, and a history of alcohol use should be actively sought. For the individual patient, if the circumstances and time course are right, any drug (including nonprescription) may be the culprit. In particular, benzodiazepines and anticholinergic medications should be suspected as one of the causes for delirium.

The physical examination should pay special attention to the evidence of infection, cardiac abnormalities, stroke, urinary retention and faecal impaction. Initial laboratory testing should include a complete blood count, electrolytes, blood urea nitrogen and creatinine levels. A urinalysis and chest x-ray may be helpful to evaluate for infection, even in the absence of fever. Toxicology screens, oximetry (or blood gas), calcium levels, thyroid hormone levels, blood cultures and an ECG may be useful if clinically indicated, or if the aetiology of the delirium remains obscure.

Although delirium is a 'brain' problem, strokes are a relatively rare cause, and can be excluded by physical examination. In a review of 127 neurology consultations for acute mental status change in one tertiary care hospital[52] the value of a thorough neurological examination for ruling out stroke was demonstrated. Of 109 patients with no focal neurological findings, only 3 (2.7%) were found to have had a stroke. Among the remaining 18 patients with focal neurological findings, 6 (33%) were believed to have an acute stroke. Overall, only 3 (2.4%) of 127 cases of delirium were believed to result from a non-obvious stroke.

Another study of 661 patients with acute stroke[53] reported that only 19 (3%) patients had delirium associated with a stroke that had no obvious focal neurological findings. Thus, while some strokes result in delirium, they typically do not do

Table IV. What to do about delirium

Goal	Action
Treat the primary disease process	
Counsel and support the patient and their family	Remind everyone that delirium is usually reversible
Avoid iatrogenic complications	Minimise medications Remove indwelling urinary catheters as soon as possible Mobilise the patient as soon as possible Ensure nutrition and fluids Treat constipation
Remove contributing factors	Metabolic (e.g. anaemia, electrolyte abnormalities) Physiological (e.g. hypoxaemia, heart failure, pain) Pharmacological (e.g. opioid analgesics, benzodiazepines, antipsychotics)
Maintain behavioural control	Provide orientation Social restraint, not mechanical or pharmacological

so in the absence of other clinical findings. Interestingly, strokes without focal findings that are responsible for delirium are typically nondominant parietal lobe or bilateral occipital lobe infarcts.[53] Thus, because it is very uncommon for a stroke to cause delirium in the absence of other findings, a computerised tomography (CT) scan of the brain is generally not required for the initial evaluation of delirium in the absence of recent head trauma, anticoagulant therapy or abnormal neurological examination. Similarly, an electroencephalogram and lumbar puncture are usually not necessary unless a cause of the delirium cannot be found after initial testing, or focal findings such as seizure activity or meningismus are present.

5. Management

The successful management of delirium, as outlined in table IV, consists of:

- avoiding complications of hospitalisation
- treating the primary condition leading to delirium
- removing contributing factors
- maintaining behavioural control
- supporting the patient and their family.

Delirious patients are particularly vulnerable and must be given special care. This requires an interdisciplinary effort by physicians, nurses, family members and anyone who comes in contact with the patient. Proper care of the delirious patient is very labour-intensive. However, failure to invest the time and effort in caring for the patient may result in additional costly and potentially life-threatening complications, and long term loss of function. A multifactorial approach to delirium, addressing a wide range of issues, is often successful because many factors typically lead to delirium; thus, multiple interventions, even if individually small, may lead to marked clinical improvement.

Delirious patients are susceptible to a wide range of iatrogenic complications, and careful surveillance to avoid potential problems is critical. Bowel and bladder function should be monitored closely, but urinary catheters, which can lead to urinary tract infection, should be avoided unless absolutely required for monitoring fluids or treating urinary retention. Bulk laxatives can be used to prevent constipation, particularly in patients who are concomitantly using opioid analgesics. Complete bedrest should be avoided as it may lead to increasing disability through the disuse of muscles, the development of pressure ulcers and atelectasis in the lungs. Exercise and ambulation prevent the deconditioning often associated with hospitalisation. Malnutrition can be avoided through the use of nutritional supplements and careful attention to the intake of food and fluids. Some delirious patients may need assistance with feeding.

Treating the primary illness may lead to a resolution of delirium, and should be attempted whenever possible. In addition, some causes of delirium have specific treatments. For example, in severe delirium attributable to anticholinergic agents, the central acetylcholinesterase inhibitor physostigmine may be tried, provided that careful attention is paid to peripheral cholinergic toxicities such as arrhythmias, salivation, diarrhoea and nausea.[54] The efficacy of other, less toxic, central cholinesterase inhibitors (e.g. donepezil and tacrine) in the setting of anticholinergic delirium, has not been

studied, but cholinergic delirium from tacrine has been reported.[55]

In alcohol withdrawal, a recent meta-analysis suggested that benzodiazepines are more effective than antipsychotics in reducing delirium.[56] Although not in use in the US, clomethiazole (chlormethiazole), a hynosedative with a similar structure to thiamine (vitamin B_1), is commonly used to treat alcohol withdrawal.[57]

Pimozide, a diphenylbutylpiperidine antipsychotic that is often used to control the motor and phonic tics associated with Tourette's disorder, is also a potent calcium antagonist and has been reported to alleviate delirium secondary to hypercalcaemia.[58] The progesterone receptor antagonist mifepristone has been reported to reverse the psychosis associated with Cushing syndrome.[59]

Unfortunately, with the exception of alcohol withdrawal, well-designed randomised trials of drug treatments for delirium do not exist. Moreover, a great deal of delirium is not attributable to a specific treatable aetiology, especially in the elderly. Although the neuropathophysiology of delirium is an area of intense interest,[60] studies in this area have not yet led to specific treatment recommendations for most patients with delirium.

While removing all of the factors that could potentially contribute to delirium may seem a daunting task, it is as important as treating the primary condition that is causing the delirium. Some factors, such as age and prior cognitive impairment, are not modifiable. In practice, the major reversible contributors to delirium are generally metabolic, physiological or pharmacological in nature. Common metabolic abnormalities, such as hyponatraemia, hypernatraemia and anaemia, should be corrected whenever possible. Common physiological derangements, such as hypoxaemia, dehydration and uncontrolled pain, must also be addressed. Drugs that contribute to delirium (table III) should be replaced with drugs that have no central adverse effects. For example, histamine H_2 receptor antagonists may be replaced by sucralfate in some patients, and the regular use of paracetamol (acetaminophen) 3 to 4 times daily may reduce or eliminate the need for opioids in many patients.

Maintaining behavioural control while ensuring both the comfort and safety of the patient can be challenging. The patient should be placed in a room near the nursing station so that close observation can be provided. Nonpharmacological behavioural control measures provide orientation and a feeling of safety. Orienting items such as clocks, calendars and even a window view should be visible. Patients should be encouraged to wear their glasses and hearing aids.

Although the use of physical restraint has not been well studied in the inpatient setting, evidence from long term care suggests that restraints probably do not decrease the rate of falls in confused ambulatory individuals,[61] and may actually increase the risk of fall-related injury.[62] Restraints, while objectionable, may be required because of violent behaviour, or to prevent the removal of important devices such as endotracheal tubes, intraarterial devices and catheters. In such cases it is important to continually reassess the indication for the restraints, and remove such devices (and thus the indication for the restraints) as soon as possible. Even in individuals with these devices, the calm reassurance provided by a sitter or family member may be much more effective than restraints or drugs.

Pharmacological restraints are also often used as 'time-savers', but they extract a particularly costly toll in terms of physical accidents, adverse effects and loss of mobility, and should be avoided if possible. Chemical intervention may be necessary for symptoms such as delusions or hallucinations that are frightening to the patient when verbal comfort and reassurance are not successful. Some delirious patients display behaviour that is dangerous to themselves or others, and providing a sitter or family companionship is ineffective or impossible. However, the mere presence of delirium is not an indication for pharmacological intervention. Indications for such interventions should be clearly identified, documented and constantly reassessed.

In such situations, high potency antipsychotics are preferred because of their low anticholinergic activity and minimal hypotensive effects. However, these medications must be used cautiously as they may actually prolong delirium, and may increase the risk of complications by converting a hyperactive, confused patient into a stuporous one whose risk of falling or aspiration may be increased. In elderly patients with mild delirium, low doses of haloperidol (0.25 to 0.5mg orally or 0.125 to 0.25mg parenterally) should be used initially, with careful reassessment before giving additional doses. In more severe delirium, somewhat higher initial doses may be used (0.5 to 2mg parenterally), with additional doses every 30 to 60 min as required.

Care must be taken to assess the patient for akathisia (motor restlessness), which may be an adverse effect of high potency antipsychotics and can be confused with worsening delirium. The treatment for akathisia is less, not more, antipsychotic medication. Because of its extrapyramidal adverse effects, haloperidol should be avoided in elderly persons with parkinsonism, and a benzodiazepine such as lorazepam may be substituted. One recent report[63] suggested that low doses of the atypical antipsychotic agent risperidone may also be effective in delirium.

High dose intravenous haloperidol may be the treatment of choice in critically ill intensive care unit patients.[64] In such patients, the risk : benefit ratio of adverse drug reactions versus the removal of lines and devices often favours pharmacological treatment. Such therapy must be used with special caution in older individuals. In addition to extrapyramidal effects, the potential for QT interval prolongation and torsades de pointes,[65] neuroleptic malignant syndrome[66] and withdrawal dyskinesias[67] remain important concerns. As with mechanical restraints, in all cases where pharmacological restraints are used the healthcare team must clearly identify the target symptoms necessitating their use, frequently review the efficacy of the sedative or antipsychotic agent in controlling the target symptoms, and assess the patient for adverse effects and complications.

Sleep-wake cycle alterations during delirium may be of concern to patients, their families and the medical team. Overaggressive pharmacological treatment of sleep disturbance should be avoided. Some patients may have diagnosed or undiagnosed sleep apnoea, and sedatives would more likely worsen than improve the sleep disturbance. Furthermore, one study of 27 post-cardiotomy patients[68] found that insomnia in the immediate postoperative period correlated best with confusion during the prior day, suggesting that the sleep disturbance resulted from the delirium, and not vice versa.

Finally, it is important to stress to family members that delirium is usually not a permanent condition, but rather improves over time. Unfortunately, the persistence of delirium is common. One study of 110 delirious patients at a tertiary care hospital[1] found that only 4% experienced resolution of all new symptoms of delirium by the time they were discharged from hospital. Six months after discharge, resolution of all new symptoms of delirium was not complete in 57.5% of the patients. The persistence of delirium symptoms was confirmed by another study of 173 patients in a geriatric assessment unit in the Canadian province of Nova Scotia.[69] Of the 43 (25%) patients with delirium, complete symptom recovery occurred in only one-half of the surviving patients at hospital discharge (mean length of stay 32 days). Thus, when counselling families it is important to point out that many cognitive deficits associated with the delirium syndrome can continue to abate even weeks and months following the illness.

6. Conclusion

We propose that the best way to manage delirium is to prevent it before it happens. This may be impossible in some cases, but many cases of delirium may be preventable. As in all prevention, the clinician must first think about delirium before it happens. The clinician must also know their patient's baseline cognitive and physical functioning,

medications and vulnerabilities. Very old patients (>80 years), patients with sensory, cognitive and functional impairments, and those with multiple chronic medical problems who are taking medications are at highest risk. These high risk patients are also more likely to be exposed to the precipitants of delirium, and the clinician must attempt to prevent this by recognising and treating illnesses early, minimising exposure to medicines, providing appropriate treatment environments, and attending to nutrition and mobility.

Management should focus on improving the condition(s) precipitating the delirium, providing support to the patient and their family, avoiding complications of hospitalisation, removing contributing factors and maintaining behavioural control. Sedation and restraints should be avoided, if possible. In short, the clinician should treat the delirium before it begins. Paradoxically, it is only by understanding delirium, its definition, recognition, predisposing factors, contributing factors and management, that the clinician can hope to prevent it. This may indeed be the best way of avoiding its adverse clinical, functional and economic sequelae.

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Correspondence and reprints: Dr *Edward R. Marcantonio*, Research and Training Institute, Hebrew Rehabilitation Center for Aged, 1200 Centre Street, Boston, MA 02131, USA.
E-mail: marcantonio@mail.hrca.harvard.edu