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Drug-Induced Delirium
Diagnosis and Treatment

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Summary

Drug intoxication, acute illness and other stressors can produce delirium, a common complication of hospitalisation in older patients, particularly those with dementia. Because delirium is associated with a high mortality and morbidity, clinicians must recognise it and treat its underlying causes without delay.

Drugs are a leading contributor to delirium. Agents commonly linked to delirium include anticholinergic drugs, hypnosedatives, analgesics (opioid and nonopioid), histamine H_2 receptor antagonists and antiparkinsonian drugs. Drug-drug and drug-disease interactions may also cause delirium in situations when a single drug alone would be well tolerated. For many drugs, it is not known through what mechanism they produce acute mental deterioration. Furthermore, delirium can occur despite 'therapeutic' serum concentrations.

A major challenge is excluding other medical problems. A cost-effective approach focuses on a basic clinical evaluation searching for the most common

aetiologies, such as fluid/electrolyte disturbances, infection and drug toxicity. Specialised testing such as neuroimaging is reserved for selected cases.

The key to managing delirium is to treat its underlying cause. If a medication is at fault, eliminating that agent, or substituting a less deliriogenic alternative, is needed. Delirium takes time to abate, so the patient must be kept from harm in the meantime. This includes restorative and supportive care, and control of behaviours that are harmful to the patient or others around them.

Pharmacological therapy is often used to manage delirium, but no medication used to treat delirium is entirely safe.

1. Definitions and Clinical Manifestations

The American Psychiatric Association, in DSM-IV,[1] has attempted to achieve a consensus definition of delirium based on expert opinion and recent studies. Four key features characterise delirium (table I); these are discussed in depth in sections 1.1 to 1.4.

1.1 Disturbance of Consciousness

One of the first manifestations of delirium is a change in the level of awareness and ability to focus, sustain or shift attention. This may present as a change in the *level* of consciousness: patients with delirium may appear drowsy, lethargic, even semicomatose.

The opposite extreme, hypervigilance, may occur in cases of alcohol (ethanol) or sedative drug withdrawal. If awake and calm, delirious patients appear distracted or may need to be redirected many times in order to maintain a conversation.

Table I. DSM-IV[1] criteria for delirium

A. Disturbance of consciousness (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention
B. Change in cognition (such as memory deficit, disorientation or language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia
C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate over the course of the day
D. 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, by an intoxicating substance, by medication use or by more than one aetiology

1.2 Impairment of Cognition and Perception

Delirious individuals have cognitive impairment and perceptual problems that cannot be explained by a prior or progressing dementia. Because the cognitive manifestations may resemble those of dementia, knowledge of the patient's baseline level of functioning is important.

Among the possible manifestations of delirium are short term memory deficits, disorientation, misinterpretations of the surrounding environment and language problems. Common language difficulties include problems with writing, incoherent or irrelevant speech, and perseverations.

Delirious patients may misidentify the clinician or believe that objects or shadows in the room represent a person. Vague delusions of harm often accompany these misperceptions. Visual and tactile hallucinations, although they are among the most dramatic features of delirium, are relatively uncommon.[2]

1.3 Acute Onset and Fluctuating Course

Delirium is acute (defined in DSM-IV as lasting hours to days) and varies over the course of a day (typically being worse at night). Patients with delirium can be lucid during morning rounds even if combative or confused the night before. Therefore, clinicians must rely on more than just a single point assessment if they are not to miss the problem.

Not only can consciousness and cognition fluctuate, but so can emotional state and psychotic fea-

tures. The varying character of the affective and psychotic features helps clinicians distinguish delirium from primary mood or thought disorders. Psychomotor activity also can show extreme variation, with patients appearing hyperactive one moment, then withdrawn and hypoactive the next.

One aspect of chronology that is no longer required in the DSM-IV definition of delirium is prompt reversibility. Although the disturbance of consciousness and cognition is potentially correctable when delirium is promptly recognised and its underlying cause effectively treated, a complete return to baseline may take weeks or months, or never occur at all.[3]

1.4 Medical Aetiology

Patients with delirium are sick. Although delirium has been described as 'brain failure', usually its cause lies outside of the CNS. Typical precipitants are listed in table II.

Drug toxicity accounts for approximately 30% of cases, but even when delirium is drug-induced, other medical contributors are frequently present.[4,5]

The challenge with delirium is that patients often do not look 'sick', even if serious illness, such as sepsis or myocardial infarction, is present. Short term mortality is high – approximately 14% at 1 month and 22% at 6 months following a diagnosis of delirium, an increase of more than 2-fold compared with patients without delirium.[6] This higher mortality reflects the severe underlying illness, both acute and chronic, typically present in such patients. Delirium, however benign it appears, indicates a potential medical emergency.

1.5 Other Manifestations

A reversed sleep-wake cycle is often found in delirious patients. Night-time represents the period of greatest arousal and agitation, while during the daytime patients are drowsy or lethargic. Because many other conditions (e.g. acute illness, pain, dementia) disturb sleep in older patients, this finding has less diagnostic value than the core features emphasised in DSM-IV.[2]

Table II. Medical conditions commonly causing delirium

Fluid/electrolyte disturbances
dehydration
hypo/hypernatraemia
Infections
urinary tract
respiratory tract
skin and soft tissue
Drug toxicity
Metabolic disorders
hypoglycaemia
hypercalcaemia
uraemia
hepatic insufficiency
Low perfusion states
shock
heart failure
Withdrawal from alcohol (ethanol) or sedatives

In addition to insomnia, other features of delirium can include difficulty concentrating, anxiety, restlessness, irritability, hypersensitivity to lights and sounds, and vivid dreams or nightmares.[7] Patients able to recall this phase of their delirium attest to feeling intense fear and other emotions.

Delirium is common in older patients with underlying chronic disease, the group most prone to functional decline during hospitalisation. Acute urinary incontinence and loss of the ability to perform basic self-care tasks often complicate delirium. The medical complications of immobility, such as falling, aspiration pneumonia and skin breakdown, occur more frequently in patients with delirium, often as a result of the use of chemical or physical restraint. Such factors partly explain the high risk for functional decline and institutionalisation following an episode of delirium.[8,9]

The physical signs of delirium may include autonomic nervous system activation (tachycardia, sweating, flushing, dry mouth and dilated pupils), but these responses are typically blunted or absent in older patients. Nonrhythmic muscle jerking (myoclonus) and flapping motions of an outstretched, dorsiflexed hand (asterixis) are common

features of delirium caused by metabolic disturbances.

1.6 Prevalence and Risk Factors

Prospective studies have demonstrated that, at the time of hospital admission, between 10 and 15% of older medical patients meet criteria for delirium, and that an additional 5 to 30% may develop the disorder later during hospitalisation.[5] Much less is known about the prevalence of delirium in subacute- or chronic-care settings. One study suggested 9% of nursing home residents and 16% of those in dementia special-care units had features of delirium.[10]

Multiple risk factors contribute to delirium, and the more that are present, the greater the likelihood of the condition occurring. The risk of delirium is higher in severely ill patients, patients of advanced age, those using psychoactive drugs and those with impaired physical function. The strongest and most consistent risk factor for delirium among recent studies has been the presence of underlying dementia, which increases the risk of delirium nearly 3-fold.[4,5] Other chronic brain diseases, such as parkinsonism, also increase the risk of delirium.[5]

Surgery poses a risk for delirium that is comparable to nonsurgical illness requiring hospitalisation. In some settings, such as hip fracture, the incidence of delirium is higher than 50%.[11] Risk factors for perioperative delirium include advanced age, dementia and the use of anticholinergic drugs.[12,13] Type and route of anaesthesia itself has little effect on the incidence of delirium.[13]

One of the most frequent laboratory abnormalities found in delirious patients is a low serum albumin level. This is a particularly important risk factor for drug-induced delirium, since hypoalbuminaemia can enhance CNS toxicity by leading to higher unbound concentrations of centrally acting drugs.[14]

1.7 Tips for Identifying Delirium

Although delirium is common and has a poor prognosis, recent studies show that physicians overlook the disturbance nearly half of the time.[15] Often, confusion is not evident during a brief encounter at the bedside. Even when odd or confused behaviour is recognised, clinicians may wrongly attribute it to age, dementia, fatigue or other psychiatric illness. Table III lists several recommendations for improving the identification of delirium.

A user-friendly way to screen patients for delirium is the Confusion Assessment Method.[15] This scale utilises core DSM criteria and uses a simplified diagnostic algorithm that can be rapidly completed. It comprises 4 features:

1. Acute onset and fluctuating course
2. Inattention
3. Disorganised thinking
4. Altered level of consciousness.

Delirium is suspected if features 1 and 2 and either 3 or 4 are present.

Clinicians can be easily trained to use the Confusion Assessment Method, the flexible structure of which is adaptable to many settings. This method appears to have better sensitivity and specificity for delirium than cognitive screening instruments, since it was designed to incorporate information from all available sources.[16]

Table III. Strategy for improving the recognition of delirium in older patients

Maintain a high index of suspicion
• do not treat lethargy or tangential speech as 'normal'
• when in doubt, presume delirium
Perform cognitive testing (MMSE, digit span)
• on initial encounter and whenever a change is suspected
• manner of performance is more important than 'score'
Look for clues in conversation
• does the patient have difficulty focusing attention?
• is the patient's thinking disorganised or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas or unpredictable switching from subject to subject?
• was the patient's level of consciousness abnormal?
Interview capable informants
• does the caregiver report acute change and fluctuating course?
• take subtle changes seriously
Use a team approach
• actively solicit evidence of behaviour change
• review nursing notes for after-hours confusion
• educate all team members about delirium

Abbreviation: MMSE = Mini–Mental State Examination.

2. Mechanisms of Drug-Induced Delirium

Drugs precipitate delirium in several possible ways. Centrally acting agents may be present in toxic concentrations as a result of overingestion or impaired clearance. Important pharmacokinetic changes that accompany aging, such as a reduced volume of distribution for hydrophilic agents and reduced clearance, often explain the increased risk for drug-induced delirium among older patients.

However, delirium also occurs in patients with 'nontoxic' blood concentrations of centrally active drugs (e.g. lithium, digoxin and quinidine[17,18]). Pharmacodynamic changes may result in an increased sensitivity to the effects of some drugs for any given plasma concentration.

Additionally, drug-drug or drug-disease interactions can increase the risk of delirium in individual patients. Perhaps the most important drug-disease interaction is between centrally acting drugs and dementia, where the risk of delirium is enhanced due to reduced 'cognitive reserve'. Such a situation has been well documented for anticholinergic drugs, which produce greater behavioural and cognitive effects in patients with Alzheimer's disease compared with age-matched controls.[19]

Finally, polypharmacy plays an important role. The risk for drug-induced cognitive impairment increases with the number of medications administered.[20]

The actual mechanisms whereby drugs cause delirium, however, are poorly understood, since the pathophysiology of delirium is itself poorly understood. Electrophysiological studies, including EEG and evoked-potentials, indicate that delirium is a diffuse brain disturbance that involves both cortical and subcortical structures.[5] Multiple neurotransmitter mechanisms are involved in maintaining normal arousal and alertness, but considerable evidence supports a major role for cholinergic failure in delirium. Not only does anticholinergic intoxication cause a classical delirium syndrome that is reversible with cholinesterase inhibitors, but clinical conditions known to cause delirium (such as hypoxia, hypoglycaemia or thiamine deficiency) also impair acetylcholine synthesis.

The development of a radioreceptor assay measuring muscarinic binding has allowed more precise elucidation of the mechanisms of drug-induced delirium. In both surgical and medical settings, acute confusion correlates with increased serum anticholinergic activity.[21,22] Many of the drugs causing delirium show measurable cholinergic receptor binding in this assay, even though they are not traditionally considered to be 'anticholinergic' (e.g. digoxin, lithium and histamine H_2 receptor antagonists).[23]

Other important neurotransmitters that may be affected in delirium include γ-aminobutyric acid (GABA), serotonin (5-hydroxytryptamine; 5-HT), noradrenaline (norepinephrine), dopamine, histamine, neuropeptides and adenosine. The relationship of many of these to delirium remains speculative, since none has been studied in detail in typical cases of delirium.

Finally, the mechanisms of delirium may be closely related to biochemical pathways involved in inflammatory states. Cytokines have had strong CNS effects in experimental situations.[24] Cognitive failure is one of the most consistent and frequently seen adverse effects when such agents are used therapeutically, and reverses when the agents are stopped.[25,26] The risk of developing delirium appears to be higher in those patients with underlying organic brain disease.[27] Endogenous cytokine activation is postulated to cause delirium in situations such as sepsis[28] and cardiopulmonary bypass.[29]

3. Common Drugs Causing Delirium

In this article, it is not possible to review all the potential pharmacological precipitants of delirium, since nearly every class of agent has been associated with cognitive changes in susceptible individuals. The *Medical Letter* publishes a list of drugs reported to have mental adverse effects that is updated biannually.[30] Additionally, other references can be consulted for further information.[31,32]

Most of what we know about the drugs causing delirium comes from unsystematic observations and case reports. Strict criteria for the assessment of adverse drug reactions have rarely been applied.[33] Furthermore, published studies often emphasise psychosis, agitation or mania, and less often describe acute confusional states without such startling features, although the latter are more commonly reported to adverse drug reaction databases.[34]

Systematic study of drug-induced delirium is further complicated by the multiple medical problems that delirious patients experience, making it at times difficult to determine whether a patient is delirious from a drug or the illness for which it was prescribed.

Finally, in cohort studies, it is difficult to demonstrate associations between drugs and delirium, since their effects may be idiosyncratic or subject to the intense pharmacokinetic and pharmacodynamic variability seen in older patients.

The categories of agents more commonly or strongly associated with delirium are discussed in sections 3.1 to 3.6.

3.1 Anticholinergic Drugs

Agents with antimuscarinic activity are a leading cause of drug-induced delirium. This is because cholinergic failure is a major mechanism of delirium (see section 2) and many drugs have anticholinergic properties, including tricyclic antidepressants, antihistamines and major tranquillisers (table IV).[35]

Anticholinergic toxicity in older patients, particularly those with dementia, usually presents as acute confusion without the peripheral signs of atropine poisoning (e.g. tachycardia, fever, mydriasis).[19]

Paradoxically, the relationship between anticholinergic activity and delirium is difficult to demonstrate in prospective clinical studies,[4,36] perhaps because knowing which drugs were ingested gives little indication of total anticholinergic exposure.[37] Serum anticholinergic activity measured using a radioreceptor assay provides a more accurate estimate of anticholinergic exposure, and does show a strong relationship to delirium.[21,22]

Anticholinergic delirium is the only form of delirium for which specific pharmacological therapy exists. Physostigmine, a cholinesterase inhibitor, can reverse delirium due to anticholinergic toxicity for up to 1 hour following a 1 to 2mg intravenous dose. Because of the short duration of action of physostigmine relative to the half-life of most anticholinergic agents and the potential for serious

Table IV. Medications with anticholinergic effects

Antidepressants
Amitriptyline
Desipramine
Doxepin
Imipramine
Nortriptyline
Antipsychotics
Chlorpromazine
Perphenazine
Thioridazine
Trifluoperazine
Antihistamines
Chlorphenamine (chlorpheniramine)
Cyproheptadine
Diphenhydramine
Hydroxyzine
Promethazine
Antispasmodics
Atropine
Atropine sulphate/hyoscyamine sulphate, phenobarbital (phenobarbitone)/scopolamine hydrobromide combination
Dicycloverine (dicyclomine)
Glycopyrronium bromide (glycopyrrolate)
Propantheline
Scopolamine
Antiemetics
Meclozine (meclizine)
Prochlorperazine
Thiethylperazine
Trimethobenzamide
Antiparkinsonian agents
Benzatropine
Trihexyphenidyl (benzhexol)
Cardiovascular drugs
Disopyramide
Procainamide
Quinidine

cholinergic adverse effects (e.g. bradycardia and bronchospasm), its use requires close monitoring.[38] The use of physostigmine may potentiate the toxicity of tricyclic antidepressant overdose.[39] Since most cases of anticholinergic toxicity can be safely treated by stopping the offending agent and providing supportive care, physostigmine has only limited usefulness in the treatment of delirium.

3.2 Hypnosedatives

Benzodiazepines are the most widely prescribed psychoactive drugs. They produce sedation, psychomotor slowing, postural instability and chronic cognitive impairment in older patients. These effects often persist for many days after the agents are tapered and discontinued, due to their prolonged metabolism.[40] Reports of delirium and 'paradoxical agitation' are relatively few in number and thought to occur more often with shorter-acting agents such as triazolam and alprazolam.[31]

Recent studies, however, indicate that the potential for delirium may have been underestimated. Hypnosedatives, primarily benzodiazepines, were the commonest drugs associated with cognitive impairment in older patients attending a memory clinic.[20] Recent prospective studies have demonstrated an increased risk for delirium in older hospitalised patients receiving benzodiazepines.[4,36,41] In one study, the risk for delirium showed a dose-response trend and was greater after exposure to long-acting rather than short-acting agents.[36]

Delirium may also occur in long term users of benzodiazepines as a result of withdrawal. Short-acting agents such as alprazolam are believed to confer a greater risk of withdrawal reactions, although this is based primarily on case reports.[42] One small study suggested that the abrupt withdrawal of benzodiazepines at the time of hospital admission increased the risk of acute confusion nearly 4-fold compared with other admissions. None of the confused patients, however, demonstrated autonomic manifestations of withdrawal.[43] This atypical presentation of sedative drug withdrawal makes recognition of the problem more difficult

3.3 Analgesics

Nonopioid and opioid analgesics have both been associated with delirium. Among opioids, pethidine (meperidine) appears to confer the greatest risk, due to the accumulation of its metabolite norpethidine, which has anticholinergic and CNS excitatory properties.[36] Because this metabolite is cleared renally, it is more likely to cause delirium in older patients and those with impaired kidney function.

Toxicity from aspirin (acetylsalicylic acid) and other salicylate compounds frequently manifests as delirium. In older patients, classic symptoms of salicylism, such as tinnitus, are often absent, making salicylate toxicity harder to diagnose and accounting for the high frequency of chronic salicylate intoxication.[44]

Nonsteroidal anti-inflammatory drugs (NSAIDs) have also been associated with delirium and other forms of neuropsychiatric dysfunction.[45,46] Studies have been limited to case reports, and underreporting is suspected. Because these medications as a group are the most frequently prescribed agents in current practice, the cognitive impact of NSAIDs is far from trivial. Adverse drug reaction monitoring in New Zealand, for instance, identified neuropsychiatric reactions as the third most common reaction type reported with NSAIDs.[47]

3.4 Histamine H_2 Receptor Antagonists

Because cimetidine was the first drug of its class to reach the market, it has had the greatest number of reported cases of acute confusion. However, all H_2 receptor antagonists have the potential to cause delirium and, based on reported adverse drug reactions, there is little evidence that any one agent is better tolerated than another.[34,48]

CNS toxicity generally occurs during the first 2 weeks of therapy, and has been seen most commonly in intensive care unit patients, especially those with renal or hepatic failure.[49] Healthy outpatients rarely experience acute confusion after

starting an H_2 receptor antagonist. It is reported that reactions resolve within 3 days of drug withdrawal.[48]

3.5 Antiparkinsonian Drugs

A variety of behavioural disturbances, including visual hallucinations, delusions, mood changes and acute confusional states, occur as a complication of the drug treatment of Parkinson's disease.[50] All drug categories, including anticholinergic agents, amantadine, levodopa preparations and direct-acting dopaminergic agonists, have the potential to cause the delirium syndrome. Monoamine oxidase inhibitors such as selegiline (deprenyl) are usually benign when used alone, but may potentiate the neuropsychological effects of other antiparkinsonian agents.[51]

The greatest risk for delirium is in older patients, those with dementia and those receiving anticholinergic drugs.[50]

If a patient develops delirium while on antiparkinsonian therapy, the first step is to discontinue anticholinergic agents and amantadine because they confer the highest risk for delirium (see section 3.1) and have the least impact on motor function. The next step should be discontinuing selegiline and reducing or discontinuing dopamine agonists. Levodopa reductions should be made cautiously, since abrupt discontinuation may precipitate a neuroleptic (antipsychotic) malignant-like syndrome.[51]

Drug-induced delusions or hallucinations that do not respond to such conservative measures may respond to low doses of clozapine, an antipsychotic agent associated with a low incidence of extrapyramidal effects.[52]

3.6 Miscellaneous Agents

A variety of drugs in differing medication classes have been associated with delirium in multiple case reports.

Digitalis delirium has been frequently reported and often manifests with a depressed mood. Such toxicity occurs even in patients with 'therapeutic' concentrations.[17] Delirium occurs with other cardiovascular drugs, particularly antiarrhythmics[53] and β-adrenoceptor blockers.[54]

Antibiotics are seldom reported to cause delirium unless there is unusually high CNS exposure (e.g. intrathecal or intraventricular administration, or accumulation in renal failure).[55] Under-reporting is likely, because it is difficult in seriously ill patients to separate the effect of infection and fever from that of the drug. Delirium has been observed in less ill patients taking oral antibiotics such as ciprofloxacin and trimethoprim-sulfamethoxazole. These reports have generally involved older patients and those with HIV infection.[56,57] Underlying dementia in both of these settings may have increased the susceptibility to these agents.

All antiepileptic drugs can produce cognitive adverse effects including delirium, although the risk is low when blood concentrations are in the standard therapeutic range.[58] It is important to rule out post-ictal confusion before attributing cognitive changes to these agents.

Corticosteroids have been associated with delirium and psychosis, particularly in the early years of their use. Reports are much less common with prednisone than with high-dose cortisone or corticotrophin (adrenocorticotropic hormone; ACTH). Often affective features are quite prominent, leading to a diagnosis of mania or depression.[59,60] High doses, female gender and a recent change in dose (increase or decrease) have been reported to increase the risk of delirium.[59,60] Steroid psychosis responds to gradual reduction of dosage and low-dose antipsychotics. Tricyclic antidepressants have been reported to exacerbate the clinical state and should be avoided.[61]

4. Managing Delirium

The management of delirium is based on clinical experience rather than systematic studies.[5,15] The basic principals are:

- identifying and treating acute precipitants
- providing supportive and restorative care
- controlling disruptive behaviours with a minimum of chemical or physical restraint.

4.1 Evaluating Acute Precipitants

Prompt treatment is needed to reverse the effects of delirium. A prudent approach is to use a stepwise evaluation (fig. 1), starting with quick, basic tests meant to uncover the most probable aetiologies. More sophisticated or time consuming testing should be reserved and based on clinical suspicion and the patient's response to initial therapy.

A very effective initial step is to review the medication list. Often a drug with the potential to cause delirium is obvious, and a trial of eliminating it and all other unnecessary medication serves both a diagnostic and therapeutic purpose. When a certain class of drug is essential, substituting an alternative with less deliriogenic potential is wise (e.g. morphine instead of pethidine). It is also important to consider the possibility of unseen medications. Alcohol or sedative drug withdrawal may not be obvious. Additionally, over-the-counter drugs, drugs prescribed by other physicians, or drugs belonging to other household members may be a potential cause of delirium.

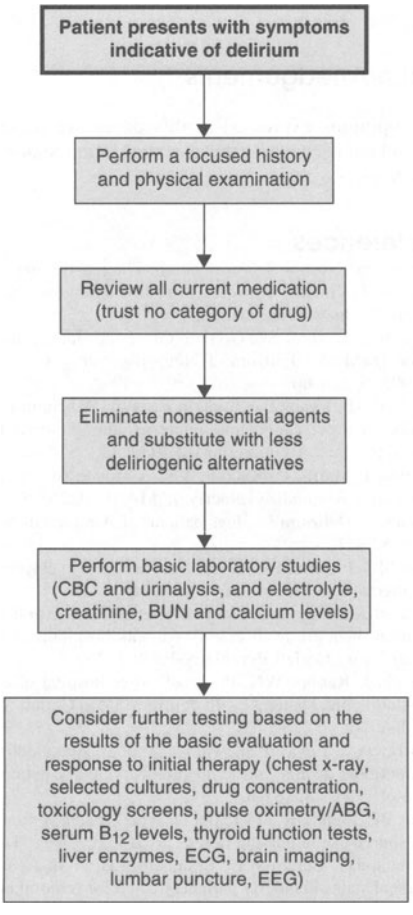

Fig. 1. Stepwise evaluation of delirium. *Abbreviations:* ABG = arterial blood gases; BUN = blood urea nitrogen; CBC = complete blood counts.

Neurological examination is helpful in identifying those patients with delirium who need immediate neuroimaging. Visual fields should be tested whenever possible, since hemianopsia may be the only clue of a posterior cortical stroke presenting as delirium with no motor findings.[62] Neuroimaging should be obtained immediately if there is a new focal neurological finding or recent head trauma, but should be used selectively in other situations.

Bacterial meningitis is a comparatively uncommon cause of delirium. Nuchal rigidity, when present, does not increase the likelihood of meningitis, since cervical arthritis or other neurological illness may mimic this finding. In febrile older patients with delirium, routine evaluation of the CSF is not necessary so long as other infectious foci are evident.[63]

EEG has a long tradition of use in delirium. However, it is rarely needed to make a diagnosis of delirium, as the clinical criteria are quite sensitive themselves. Also, a single EEG in a patient with mild delirium has poor sensitivity.

4.2 Supportive and Restorative Care

The delirious patient is at risk for dehydration, malnutrition, aspiration pneumonia, pressure ulcers, deconditioning, isolation, untreated pain, and other complications of immobility and confusion. Attention to these factors may improve the functional outcomes of an episode of delirium.

Interpersonal and environmental manipulations are often sufficient to control disruptive behaviours. Frequent reassurance and touch and verbal

orientation from familiar persons can lessen disturbed behaviours. The hospital environment is often an iatrogenic source of worsening confusion. Ambient noise, poor lighting, lack of windows, room changes and use of restraints can contribute to confusion and agitation. Constant observation ('sitters') may be cost-effective for selected patients with severe disturbances and will avoid complications associated with physical restraints.

A final aspect of supportive care is a comprehensive assessment to identify long term needs. Often delirium is the 'last straw' for caregivers of demented elderly. Although institutional care may be necessary for the delirious patient who is functioning poorly, such decisions should be made cautiously, since delirium may require weeks or months to resolve.

4.3 Controlling Disruptive Behaviours

When prompt symptom control is needed to prevent harm and to allow evaluation and treatment, psychotropic medications may be required. Unfortunately, there is no ideal drug for controlling delirium.

Haloperidol, administered at an initial dose of 0.5 to 1.0mg orally, intramuscularly or intravenously, is usually well tolerated even in critically ill patients, and has few anticholinergic or hypotensive effects. However, older patients with dementia are more likely to experience adverse extrapyramidal effects with potent antipsychotic agents. Akathisia resulting from haloperidol may be mistaken for delirium, leading to an escalating cycle of drug administration. Neuroleptic malignant syndrome may also occur in older patients receiving short term treatment with antipsychotics for agitation.

Benzodiazepines (e.g. lorazepam 0.5 to 1.0mg) have a more rapid onset of action (1 to 5 minutes after intravenous administration) than antipsychotics, but peak effects are brief and sedation is more common. They are the drugs of choice to treat sedative drug and alcohol withdrawal, and can be useful as adjuncts to antipsychotics, where they promote sedation and may reduce extrapyramidal adverse effects.

5. Conclusion

Delirium is a serious and common complication of acute illness, and drugs are a leading contributor to the phenomenon. Identifying and eliminating those drugs is essential, but not sufficient. Equally important is paying attention to the patient's other needs, such as managing acute illness and assessing chronic cognitive or functional impairments.

Further work is needed to elucidate the mechanisms of drug-induced delirium and to improve the outcome of patients experiencing this condition.

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