Delirium

Synonyms: acute confusional state, acute brain failure, acute organic reaction, postoperative psychosis

Delirium is a clinical syndrome which is difficult to define exactly but involves abnormalities of thought, perception and levels of awareness. It typically is of acute onset and intermittent. Both hypoactive and hyperactive delirium states are recognised and often patients exhibit features of both. Patients may appear confused or 'not with it' when talking to them. Alternatively, it may be their family or carer noticing the confusion.

It is very common - especially in the elderly - and many of these patients subsequently do not return to their baseline function, with some even requiring institutionalisation. It can occur acutely or subacutely and symptoms fluctuate. More disappointing is the realisation that delirium can be avoided in many cases (up to one third) and the lack of awareness is leading to a large amount of morbidity and mortality and a burden on NHS costs.

The terms 'prevalent delirium' and 'incident delirium' are sometimes seen in the literature. Prevalent delirium means that the condition is present on admission whereas incident delirium occurs during admission.

**Important points to remember in delirium**
- Patients are vulnerable.
- It is a common scenario for errors - eg, missing the diagnosis and poor management; it has the potential to become serious rapidly.
- Do not assume confusion is due to long-term dementia or mental handicap even in the elderly and those with learning difficulties:
  - It is important to check the previous level of function from relative/carer/home circumstances.
  - If this is not possible, treat as acute confusion until proven otherwise.
- Always perform a full physical examination, including airway/breathing/circulation and vital signs; however, bear in mind that the patient may not be able to co-operate fully.
- Always check blood glucose and pulse oximetry (also see 'Investigations', below).

**Epidemiology**

Delirium occurs in 30% of those in emergency departments. Occurrence rates vary from 11-42% and it is the most common complication of hospitalisation in the elderly population. The incidence is also higher in those with pre-existing cognitive impairment. The prevalence is higher in patients with malignancy and HIV. Despite these facts, delirium remains underdiagnosed and poorly managed - only 20-50% are recognised by healthcare professionals.

There is an increase in delirium with age: 0.4% in those over 18 years of age, 1.1% in those over 55 years of age, 13.6% in those over 85 years of age.

Furthermore, patients with delirium have longer hospital stays and a higher frequency of complications - eg, urinary incontinence, decubitus ulcers and malnutrition.

**Risk factors for delirium**

The following are risk factors which are associated with an increased risk of delirium:
- Age ≥65 years.
- Male sex.
- Pre-existing cognitive deficit - eg, dementia, stroke.
- Severity of dementia.
- Severe comorbidity.
- Previous episode of delirium.
- Operative factors - eg, type of operation - hip fracture repairs are more likely to be associated with delirium, as are emergency operations.
- Certain conditions - eg, burns, AIDS, fractures, infection, low albumin, dehydration.
- Current hip fracture or severe illness.
- Drug use (implicated in nearly half of cases) and dependence - eg, benzodiazepines.
- Substance misuse - eg, alcohol.
- Extremes of sensory experience - eg, hypothermia or hyperthermia.
- Visual or hearing problems.
- Poor mobility.
• Social isolation.
• Stress.
• Terminally ill.
• Movement to a new environment.
• ICU admission.
• Urea/creatinine abnormalities.

Usually a precipitant is required along with risk factors for delirium to occur. Further, the presence of a greater number of risk factors to begin with means that only a small precipitant is necessary to trigger delirium.

Aetiology[^4, 7, 10]

• **Acute infections:**
  - Urinary tract infection.
  - Pneumonia.
  - Sepsis.
  - Viral infections.
  - Meningitis.
  - Encephalitis.
  - Cerebral abscess.
  - Malaria.

• **Prescribed drugs:**
  - Benzodiazepines.
  - Analgesics - eg, morphine.
  - Anticholinergics.
  - Anti-convulsants.
  - Anti-Parkinsonism medications.
  - Steroids.

• **Surgical:**
  - Postoperative.

• **Toxic substances:**
  - Substance misuse or withdrawal.
  - Alcohol - acute intoxication or withdrawal.
  - Carbon monoxide (CO) poisoning.
  - Exposure to heavy metals.
  - Barbiturate withdrawal.

• **Vascular disorders:**
  - Cerebrovascular haemorrhage or infarction.
  - Cardiac failure or ischaemia.
  - Subdural haemorrhage.
  - Subarachnoid haemorrhage.
  - Vasculitis - eg, systemic lupus erythematosus (SLE).
  - Cerebral venous thrombosis.
  - Migraines.

• **Metabolic causes:**
  - Hypoxia.
  - Electrolyte abnormalities - eg, hyponatraemia and hypercalcaemia.
  - Hypoglycaemia or hyperglycaemia.
  - Hepatic impairment.
  - Renal impairment.

• **Vitamin deficiencies:**
  - Thiamine deficiency.
  - Nicotinic acid deficiency.
  - Vitamin B12 deficiency.

• **Endocrinopathies:**
  - Hypothyroidism and hyperthyroidism.
  - Hypopituitarism.
  - Hypoparathyroidism or hyperparathyroidism.
  - Cushing's disease.
  - Porphyria.
  - Carcinoid.

• **Trauma:**
  - Head injury.
• Epilepsy:
  • For example, postictally.

• Neoplasia:
  • Primary cerebral malignancy.
  • Secondaries in the brain.
  • Paraneoplastic syndromes.

• Others:
  • Urinary retention.
  • Faecal impaction.

• Multiple aetiology.
• Unknown aetiology.

The most common causes are medical conditions such as infections, medications or drug withdrawal.

Presentation

Making an accurate assessment relies on a collateral history to determine the patient's premorbid level of function. There are very useful cognitive function screening tools - eg, the abbreviated mental test score and the confusion assessment method.[1] The mental tests should be performed regularly and on all high-risk patients. However, it may not be appropriate or possible to do these tests on a sick patient.

The diagnosis of delirium is clinical. The following features may be present:

• Usually acute or subacute presentation.
• Fluctuating course.
• Consciousness is clouded/impaired cognition/disorientation.
• Poor concentration.
• Memory deficits - predominantly poor short-term memory.
• Abnormalities of sleep-wake cycle, including sleeping in the day.
• Abnormalities of perception - eg, hallucinations or illusions.
• Agitation.
• Emotional lability.
• Psychotic ideas are common but of short duration and of simple content.
• Neurological signs - eg, unsteady gait and tremor.

Only some of these symptoms may be present. The symptoms may coincide with underlying dementia - which is common. The diagnosis is still clinical and criteria are set out by the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) as illustrated in the next section.

ICD-10 definition of delirium not induced by alcohol and other psychoactive substances[11]
An etiologically nonspecific organic cerebral syndrome characterized by concurrent disturbances of consciousness and attention, perception, thinking, memory, psychomotor behaviour, emotion, and the sleep-wake schedule. The duration is variable and the degree of severity ranges from mild to very severe.

Subtypes of delirium[4]

• Hypoactive subtype - apathy and quiet confusion are present and easily missed. This type can be confused with depression.
• Hyperactive subtype - agitation, delusions and disorientation are prominent and it can be confused with schizophrenia.
• Mixed subtype - patients vary from hypoactive to hyperactive.

Assessment

• Check:
  • Airway/breathing/circulation.
  • Conscious level.
  • Vital signs - eg, pulse oximetry, pulse, blood pressure, temperature.
  • Capillary blood glucose.

• Full cardiovascular and respiratory examination.
• Full abdominal and genitourinary examination, if appropriate.
• Full neurological examination.
• Further examination depending on the suspected problem - eg, ENT or rectal examination.
There are several assessment methods available for the diagnosis of delirium. The easiest to use in the primary care setting is the Confusion Assessment Method (CAM) screening instrument.\[12\]

### Confusion Assessment Method (CAM)

To have a positive result the patient must have:
1. Acute onset and fluctuating course; and
2. Inattention (eg, 20-1 test with reduced capacity to shift attention or keep attention focused); and either
   3. Disorganised thinking (disorganised or incoherent speech) or
   4. Changed level of consciousness (usually the patient is lethargic or is in a state of stupor).

### Differential diagnosis\[13\]

Delirium is commonly mistaken for the following diagnoses:
- Dementia - for example, Lewy body type, which typically has a fluctuating course.\[2\]
- Depression.
- Bipolar disorder.
- Functional psychoses - eg, schizophrenia.

### Investigations\[12\]

These should be guided by the clinical presentation and are aimed at identifying an underlying cause of the delirium. Typical investigations that can be performed include:

- Full history, including collateral history and cognition testing - eg, mini mental state examination.
- Full examination - look for sources of infection, including the ears and throat; look for rashes, lymphadenopathy and check for constipation.
- Bloods - include FBC, U&Es and creatinine, glucose, calcium, magnesium, LFTs, TFTs, cardiac enzymes, vitamin B12 levels, syphilis serology, autoantibody screen and PSA. Creatinine is vital to obtain an estimated glomerular filtration rate (eGFR), as this may indicate impaired renal function and affect the handling of medications, and may predispose to drug-induced delirium.
- Urine dipstick testing and microscopy.
- Blood cultures and serology, if indicated.
- ECG.
- Pulse oximetry and arterial blood gas, if indicated.
- CXR and possibly abdominal X-ray, if indicated.
- Lumbar puncture may be necessary.
- Electroencephalography (EEG) - this is usually only performed if there is doubt regarding the diagnosis and shows generalised diffuse slowing in 80% of delirious patients.\[14\]

### Management\[1, 4\]

- This begins with increased awareness of delirium and regular measures of cognitive function. The underlying cause needs to be treated.
- It is common for patients with delirium to be admitted to hospital to help investigate the patient and for supportive management. However, some patients can be managed in the community and moving patients to a new environment can worsen delirium.
- In delirium, the features are fluctuating and some patients are lucid between episodes and can thus provide informed consent during these periods. However, if the patient is not able to provide informed consent then they can be treated in their best interests under common law.
- If the patient becomes violent or is a danger to themselves, it may be possible to manage them initially using verbal and non-verbal de-escalation techniques.\[15\]

But more specific to delirium, the management can be divided into:

- Supportive management.
- Environmental measures.
- Medical management.
- Management post-discharge.

### Supportive management

- Clear communication.
- Reminders of the day, time, location and identification of surrounding persons.
- Have a clock available.
- Have familiar objects from home around patients, especially glasses, walking aids and hearing aids.
- Staff consistency - both doctors and nurses.
Relaxation - eg, watch television.
Involve the family and carers.

Environmental measures
- Avoid sensory extremes (over- or under-stimulation).
- Adequate space and sleep.
- Single rooms if possible.
- Avoid speciality jargon.
- Control excess noise.
- Control room lighting and have a low-wattage bulb at night.
- Control room temperature (aim for 21-23°C).
- Use health advocates (interpreters) where needed and if possible.
- Maintain competence - eg, maintain walking in ambulant patients.
- Adequate nutrition and attention to continence.

A note on managing wandering. The delirious patient may have a tendency to wander. It is common to think of restraining and/or sedating the patient in these circumstances. However, this may only worsen the situation. The management should aim to keep the patient safe using the least restrictive management - eg, think of causes of agitation or wandering (eg, need for the toilet). These causes should be rectified; if this is not possible, using distraction may help. Relatives or carers may be helpful in this scenario.[12]

Medical management
- Using drugs to treat delirium can lead to adverse effects and worsening of delirium; therefore, careful consideration is required.
- Antipsychotics have beneficial effects in selected patients, particularly those who are aggressive and do not respond to verbal and non-verbal de-escalation techniques.
- Haloperidol or olanzapine are preferred, using the lowest possible dose for the shortest possible time (normally a week or less). The dose should be titrated gradually until symptoms are controlled. It should be noted that neither drug has a UK licence for this use so normal considerations regarding the use of unlicensed medicines should apply. Note that both drugs have the potential to cause extrapyramidal side-effects and should be used in caution or avoided altogether in some patients (eg, people with Lewy-body Parkinson's disease).
- In delirium resulting from alcohol withdrawal (delirium tremens), a benzodiazepine such as diazepam or chlordiazepoxide is preferred. The benzodiazepine is usually used as a reducing course. Large doses may lead to sedation and therefore close observation is required. See also the separate Acute Alcohol Withdrawal and Delirium Tremens article.

Management post-discharge
- The symptoms of delirium may last longer than the underlying condition.
- This means that some patients will be discharged with persisting abnormalities.
- These abnormalities include disorientation, inattention and depression.
- Families and carers may also need to be supported and given advice and reassurance.

Drug-induced delirium[6, 16]
Drug-induced delirium is very common amongst the elderly. Drugs can be the sole cause of delirium in some. Common drug causes of delirium include:
- Benzodiazepines.
- Narcotic analgesics.
- First-generation antihistamines.
- Antispasmodics.
- Fluoroquinolones.
- Warfarin.
- Captopril.
- Theophylline.
- Isosorbide dinitrate.
- Dipyridamole.
- Furosemide.
- Lithium.
- Tricyclic antidepressants.
- Cimetidine.
- Anti-arrhythmics.
- Statins.[17]
- Digoxin.
- Steroids.
- Beta-blockers.
- Over-the-counter medications - eg, liquid medications containing alcohol or chlorphenamine.

The role of medications may be suggested by a temporal relationship between onset of delirium and start of new medication. However, this is not always the case and practitioners need to be aware of this. Medication lists should be thoroughly reviewed in delirium. The exact mechanism of delirium is unclear but it is postulated that central cholinergic pathway blockade is a major factor.[16] This may explain why anticholinergic medications readily lead to delirious states. It may be that this factor along with the pharmacokinetic changes that occur later in life and comorbidities increase the susceptibility of elderly patients to drug-induced delirium.
Management involves stopping the offending drug; however, the actual causal medication is often unknown. In this case, all unnecessary medications should be stopped or doses reduced. These medications can be increased or re-introduced when the patient has improved. Furthermore, it may be prudent to prescribe alternatives to medications with high anticholinergic activity - eg, use of proton pump inhibitors rather than cimetidine.\[^{16}\]

**Complications\[^{16}\]**

- Hospital-acquired infections - eg, *Clostridium difficile* and meticillin-resistant *Staphylococcus aureus* (MRSA).
- Pressure sores.
- Fractures - eg, femoral or hip fractures from falls.
- Residual psychiatric and cognitive impairment.
- Some progress to stupor, coma and eventual death.

**Prognosis**

A study from the Netherlands of patients in an intensive care unit suggests that short-term delirium has no effect on mortality, whereas delirium persisting for longer than 30 days is associated with a two- to three-fold increase in mortality.\[^{18}\] Some patients may not recover for months and one third of patients will continue to have delirium. Many patients become institutionalised after delirium.\[^{2}\] A prospective cohort study in Canada discovered that symptoms of delirium persist for up to a year after an episode.\[^{19}\] The same study revealed that there was a worse prognosis if the episode has a protracted inpatient course. Patients with malignancy or HIV also have a worse prognosis.\[^{4}\]

**Prevention**\[^{1}\]**

Awareness of high-risk patients and subsequent close observation for delirium with prompt assessment and management can potentially reduce morbidity and mortality.

One study has looked at methods of reducing postoperative delirium in patients with multiple risk factors.\[^{20}\] Their results are interesting and suggest that simple factors like hyperglycaemia, poor nutritional and poor functional states (eg, delayed mobility) - all of which are easily prevented - account for adverse clinical outcomes in a subset of patients.

The National Institute for Health and Care Excellence (NICE) has thus recommended a 'tailored multicomponent intervention package' which consists of the following:\[^{1}\]

- Multidisciplinary team approach to the prevention of delirium.
- Patients should be assessed within 24 hours of admission, making note of factors that may precipitate and worsen delirium.
- There are various interventions listed in the NICE guidance, based on the identified clinical factors - for example:
  - Cognitive impairment or disorientation - provide appropriate lighting and regularly orientate the person.
  - Hypoxia - identify and correct with the appropriate amount of oxygen.
  - Pain - assess verbally and non-verbally and treat.
  - Medications - should be reviewed on a daily basis and non-essential medication stopped.
  - Other factors include dehydration, constipation, reduced mobility, infection, poor nutrition, sensory impairment and sleep disturbance.

Further education of medical staff and awareness are required.\[^{21}\] Guidelines may be effective in the management of delirium. This has been studied by one group and they reported that guidelines reinforced by teaching sessions are effective - although statistical significance was not reached.\[^{22}\]

**Further reading & references**

1. Delirium; NICE Clinical Guideline (July 2010)
12. The prevention, diagnosis and management of delirium in older people; Royal College of Physicians (2006)


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