

Delirium: Diagnosis, Aetiopathogenesis and Treatment

Delirium is a richly varied syndrome of cognitive and behavioural features which may co-exist with other somatic and mental disorders. As there is currently no diagnostic test and no reliable biomarkers have yet been identified, delirium remains a clinical diagnosis. A high index of clinical suspicion may be required in order to make the diagnosis, which should probably be considered in any patient labelled as confused (a term frequently used but with variable meaning¹), vague, uncooperative, rambling, agitated, or unable to give a coherent history.

Diagnosis and differential diagnosis

Both the Diagnostic and Statistical Manual (DSM) and the International Classification of Diseases (ICD) have diagnostic criteria for delirium.

DSM-IV-TR recognises four diagnostic categories:

- Delirium due to a medical condition
- Substance-induced delirium: due to intoxication or withdrawal
- Delirium due to multiple aetiologies
- Delirium not otherwise specified

Three common diagnostic criteria are required:

- Disturbance of consciousness:

This may encompass both quantitative and qualitative aspects of consciousness, hence “level” (= arousal, alertness, vigilance) and “intensity” (= selective attention) of consciousness; reduced clarity of awareness of environment; reduced ability to focus, sustain, or shift attention. Disordered attention may be evident clinically as increased distractibility.
- Change in cognition:

This may manifest as disorientation, language disorder, memory deficit, perceptual disturbance (illusions, hallucinations). These features should not be better accounted for by dementia.
- Development/Course:

Onset over a short period of time (hours, days) with fluctuation during the course of the day. Disturbance of sleep/wake cycles is typical, often with worsening of symptoms at night (“sundowning”).

In addition there may be diagnostic criteria by category, based on evidence from the clinical history, examination, or investigations, of a general medical condition; substance intoxication, medication use related to disturbance; more than one aetiology; or insufficient evidence for any of the above.

In ICD-10, the requirements for diagnosis are similar, and include:

- Impairment of consciousness and attention
- Global disturbance of cognition
- Psychomotor disturbance
- Disturbance of sleep-wake cycle
- Emotional disturbances

A brief consideration of these diagnostic criteria will indicate the potential clinical heterogeneity of delirium. However, two principal subtypes of delirium are described. The less common, but more easily recognised, is characterised by agitation or hyperactivity. The more common, but insidious, “quiet” variant, characterised by hypoactivity, withdrawal, and apathy, may be easily overlooked and/or misdiagnosed as depression. Not surprisingly, it is the latter form of delirium which has a poorer outcome.

Rating scales have been developed which may be helpful in screening for the diagnosis, such as the Delirium Rating Scale (DRS), the Confusion Assessment Method (CAM), and the Neecham Confusion Scale (NCS); or for measuring the severity of delirium, such as the Confusional State Evaluation (CSE) and the Delirium Severity Scale (DSS).

The differential diagnosis of delirium includes:

- Dementia
- Aphasia (especially Wernicke’s aphasia)
- Psychiatric disorders:
 - schizophrenia
 - depression/mania
 - attention deficit disorder

Many texts include tables which list the factors differentiating delirium from dementia, for example in terms of onset (acute vs. insidious), course (fluctuating vs. stable), and duration (hours/days vs. months/years). However, it is of crucial importance to recognise that the two conditions show significant overlap, dementia being an important predisposing factor for the development of delirium, and delirium sometimes being the presenting feature of dementia.^{2,3} In any elderly person developing delirium, the possibility of an underlying diagnosis of dementia must be considered. However, meaningful assessment of cognitive functions to confirm or refute a diagnosis of dementia cannot be undertaken whilst delirium persists, because of the impairments of consciousness and attention.

Epidemiology, aetiology, pathogenesis, investigation

Delirium is common, more so in hospital in-patients (the subjects of the majority of studies) than in the community. In medical in-patients, prevalence of delirium may be 10-20%, and incidence 5-10%. In surgical patients, the incidence may be up to 30%. Certain types of surgery seem particularly associated with delirium, especially cardiac and orthopaedic (especially hip fracture surgery).

Studies have identified a number of factors which may contribute to the aetiology of delirium. These may be conveniently classified as predisposing and precipitating.

Predisposing factors include:

- Age: frailty, physiological age, rather than chronological age *per se*;
- Sex: men > women;
- Neurological illness: dementia;
- Burden of co-morbidity; dehydration;
- Drugs: especially anticholinergics;
- Visual, hearing impairment.

Precipitating factors include:

- Medications: benzodiazepines, opiates
- Intercurrent illness:
 - Infection: systemic, focal (CNS)
 - Metabolic: hypoglycaemia, hypoxia
 - CNS disorders: head injury, epilepsy, inflammatory
- Iatrogenic events: surgery

A multifactorial model of pathogenesis suggests an inverse relation between pre-existing vulnerability (predisposing factors) and the severity of insult (precipitating factors) required to initiate delirium.

The pathophysiology of delirium is an area of much research. It is believed that diverse aetiologies may



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Box 1: Suggested investigations in delirium

Bloods:	FBC, ESR, film; U+Es, glucose, LFTs, thyroid function, Ca ²⁺ + Po ₄ ; blood cultures; arterial blood gases; +/- toxicology
Urinalysis	
Imaging:	CXR CT brain
CSF:	cell count, glucose, protein, Gram stain; +/- Ziehl-Neelsen stain, culture, oligoclonal bands
Neurophysiology:	EEG: degree of slowing correlates with clinical state

converge on a “final common neural pathway”, involving in particular the prefrontal, parietal, and fusiform (especially right), cortices. The factors implicated include excessive stress response, mediated by the hypothalamo-pituitary-adrenal axis; imbalance of neurotransmitters, most particularly reduced acetylcholine and increased dopamine; and immunological factors such as cytokines (increased TNF-alpha, reduced IGF-1, somatostatin)⁵.

The aetiological formulation into precipitating and predisposing factors guides the approach to investigation. The aim should be to identify any possible precipitating factors, such as an underlying medical disorder (Box 1, above).

Treatment and prognosis

Specific treatment may be instituted if delirium is diagnosed early and an underlying aetiology or precipitating cause is identified, such as a medical condition (infection, metabolic disturbance), substance misuse, iatrogenesis (use of certain medications).

More general measures must not be overlooked, such as maintenance of fluid intake and nutrition. If spectacles and/or hearing aids are normally worn they should be provided, after ensuring that they are in working order, to minimise sensory deprivation and the potential for misinterpretation of sensory stimuli. Environmental modulation, to avoid under- or over-stimulation, is recommended⁵, but is often impractical on general medical and surgical wards. Relatives and friends may visit regularly, to encourage orientation. Sleep should not be disturbed if possible.

Drug therapy is not mandatory, with the possible exception of hyperactive patients who are deemed at risk of harm to themselves or others. There is currently little trial data to guide drug use. The options include neuroleptics, either traditional D2 receptor antagonists, such as haloperidol, or newer atypical antipsychotics; or benzodiazepines, such as lorazepam. The neuroleptics appear to be superior, and early regular low dose therapy may be the most appropriate usage. It has been suggested that cholinesterase inhibitors, licensed for the treatment of Alzheimer's disease, may have a role but the available data are currently anecdotal.

The prognosis of delirium is generally good if the condition is recognised and treated appropriately. However, long term complications such as functional decline, institutionalisation, and increased mortality are recognised. Prognosis is worse if no underlying cause is found. The possibility that underlying dementia may “emerge”, having been “unmasked” by the delirium, must be borne in mind.

Following the adage that prevention is better than cure, an intervention trial in hospital in-patients at high-risk

for delirium showed that a strategy of repeated reassurance and patient orientation, early mobilisation, provision of hearing aids and glasses, avoidance of dehydration and non-pharmacological sleep promotion, reduced the incidence and duration of delirium⁶. This has rightly been hailed as a landmark trial. Furthermore, in light of these findings, it has been argued that the incidence of delirium is a marker of the quality of hospital care⁷.

Further Reading

American Psychiatric Association. *Practice guideline for the treatment of patients with delirium*. Am J Psychiatry 1999;156(5Suppl):1-20.

Andrefsky JC, Frank JI. *Approach to the patient with acute confusional state (delirium/encephalopathy)*. In: Biller J (ed.). *Practical neurology* (2nd edition). Philadelphia: Lippincott Williams & Wilkins, 2002:3-18.

Brown TM, Boyle MF. *Delirium*. BMJ 2002;325:644-647.

Burns A, Gallagley A, Byrne J. *Delirium*. J Neurol Neurosurg Psychiatry 2004;75:362-7.

Caracini A, Grassi L. *Delirium: acute confusional states in palliative medicine*. Oxford: OUP, 2003.

Lindesay J, Rockwood K, Macdonald A (eds.). *Delirium in old age*. Oxford: OUP, 2002.

Meagher DJ. *Delirium: optimising management*. BMJ 2001;322:144-149.

Nayeem K, O'Keeffe ST. *Delirium*. Clin Med 2003;3:412-415.

Taylor D, Lewis S. *Delirium*. In: Hughes RAC (ed.). *Neurological emergencies* (2nd edition). London: BMJ Publishing, 1997:76-101.

References

1. Simpson CJ. *Doctors' and nurses' use of the word confusion*. Br J Psychiatry 1984;145:441-443.
2. Robertsson B, Blennow K, Gottfries CG, Wallin A. *Delirium in dementia*. Int J Geriatr Psychiatry 1998;13:49-56.
3. Rockwood K, Cosway S, Carver D *et al*. *The risk of dementia and death following delirium*. Age Ageing 1999;28:551-556.
4. Broadhurst C, Wilson K. *Immunology of delirium: new opportunities for treatment and research*. Br J Psychiatry 2001;179:288-289.
5. Meagher DS, O'Hanlon D, O'Mahoney E, Casey PR. *The use of environmental strategies and psychotropic medication in the management of delirium*. Br J Psychiatry 1996;168:512-515.
6. Inouye SK, Bogardus ST Jr, Charpentier PA *et al*. *A multi-component intervention to prevent delirium in hospitalised older patients*. N Engl J Med 1999;340:669-676.
7. Inouye SK, Schlesinger MJ, Lydon TJ. *Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care*. Am J Med 1999;106:565-573.

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