WHAT IS DELIRIUM?

Delirium is an acute but reversible disorder of brain function and fluctuation from the baseline mental status. It has 3 classic elements to its diagnosis:

1. INATTENTION
2. DISORGANIZED THINKING
3. FLUCTUATION OF CONSCISOUSNESS LEVEL

INATTENTION

Patients with delirium do not have normal awareness of their environment.

- (•) True
- ( ) False

Correct. The cardinal features of delirium are a lack of clarity of awareness of the environment, a reduced ability to focus, and reduced ability to sustain attention or shift in between different stimuli. These are features of inattention.

DISORGANISED THINKING

Patients with delirium usually have an impaired memory

- (•) True
- ( ) False

Correct. Memory deficits are a common feature of delirium. The change in cognition that characterises delirious patients also includes disorientation and language disturbance. The inability to think clearly and perceive surroundings normally both contribute to the occurrence of hallucinations and delusional thoughts (thoughts that are incorrect or unreal but seem real to the patient). These are all features of disorganised thinking.

FLUCTUATING LEVEL OF CONSCIOUSNESS

Patients with delirium may be intermittently comatose or unresponsive

- (•) True
- ( ) False

Correct. A cardinal feature of delirium is fluctuation of conscious level. In unconscious ICU patients it is sometimes difficult to distinguish the effects of sedative drugs, the underlying disease (for example encephalopathy secondary to sepsis or liver failure), and altered consciousness from delirium. Minimising the use of sedation makes it easier to assess the contribution of delirium and encephalopathies.

TYPES OF DELIRIUM

There are **3** types of delirium:

- Hyperactive - patient displays agitation
- Hypoactive - patient may appear calm and withdrawn
- Fluctuating pattern - a mixture of hypo- and hyperactive patterns.

TYPES OF DELIRIUM

Patients with delirium are usually agitated.

True

False

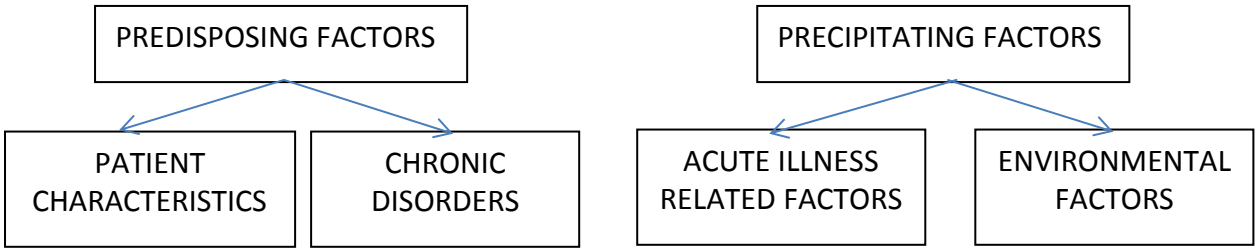
Correct. Agitation is a feature of delirium but only about 10% of ICU patients have agitated delirium. These patients often appear anxious, fearful, or sometimes euphoric. Patients with agitated delirium may be more likely to have delusions and hallucinations. The majority of patients have hypoactive delirium or a mixed/fluctuating pattern. Patients with hypoactive delirium are frequently unrecognised unless screening tests are used regularly. They often appear sedated and confusion is a common feature.

FREQUENCY AND RISK FACTORS FOR DELIRIUM IN ICU

Delirium is frequently undiagnosed and unrecognised in ICU patients. When screened for carefully, studies show that up to 80% of mechanically ventilated adult ICU patients suffer delirium at some time.

Delirium is often only recognised when sedative drugs are reduced. Trends towards using less sedation in ICU may explain why delirium is becoming more recognised in the critically ill patients.

There are many factors that have been associated with an increased prevalence of delirium in general ward and ICU patients. A useful way of remembering these factors is to consider them under the following headings:



PATIENT CHARACTERISTICS	CHRONIC DISORDERS	ACUTE ILLNESS RELATED FACTORS	ENVIRONMENTAL FACTORS
Smoking	Chronic respiratory Disease	Sepsis	Lack of normal light
High alcohol intake	Pre-existing Hypertension	Hypoxia	Isolation
Older age	Psychoactive Medication	Pain	Low number of visitors
	Chronic cardiovascular Disease	Benzodiazepine use	Use of physical restraint
		Higher illness severity	Prolonged immobilization
		Electrolyte disturbances	Excessive noise
		Longer ICU stay	
		Sleep deprivation	
		Coma	
		Steroid administration	
		Acute renal failure	

IMPACT OF DELIRIUM ON ICU PATIENT OUTCOME

Delirium is associated with a wide range of important adverse effects. These can be usefully considered as *clinical* and *economic* outcomes. It is currently unclear whether interventions aimed at reducing the prevalence of delirium can reduce these adverse effects.

Impact of Delirium on ICU Patient Outcome

Clinical outcomes

- Higher short and long term mortality
- Greater post-ICU cognitive impairment

Economic outcomes

- Longer duration of ventilation
- Longer ICU and hospital stay
- Higher overall illness cost

HOW TO PREVENT DELIRIUM

There is no strategy or treatment to completely prevent delirium, but delirium can be decreased by trying to reduce the risk factors for delirium.

Most of these relate to:

- Avoiding drugs that increase delirium risk (eg. Long acting benzodiazepines)
- Treating drug withdrawal (eg. Alcohol; nicotine; opiate)
- Improving the environment (eg. Natural light; reduced noise; promoting sleep)
- Ensuring patient orientation (eg Use of clocks; verbal reassurance and reorientation)

HOW TO RECOGNISE DELIRIUM

Delirium, especially hypoactive delirium, is commonly missed in ICU patients. This is important because delays and failure in recognition of delirium are associated with worse patient outcomes.

Delirium can be detected in both intubated and non-intubated patients using valid and reliable tools.

Key point:

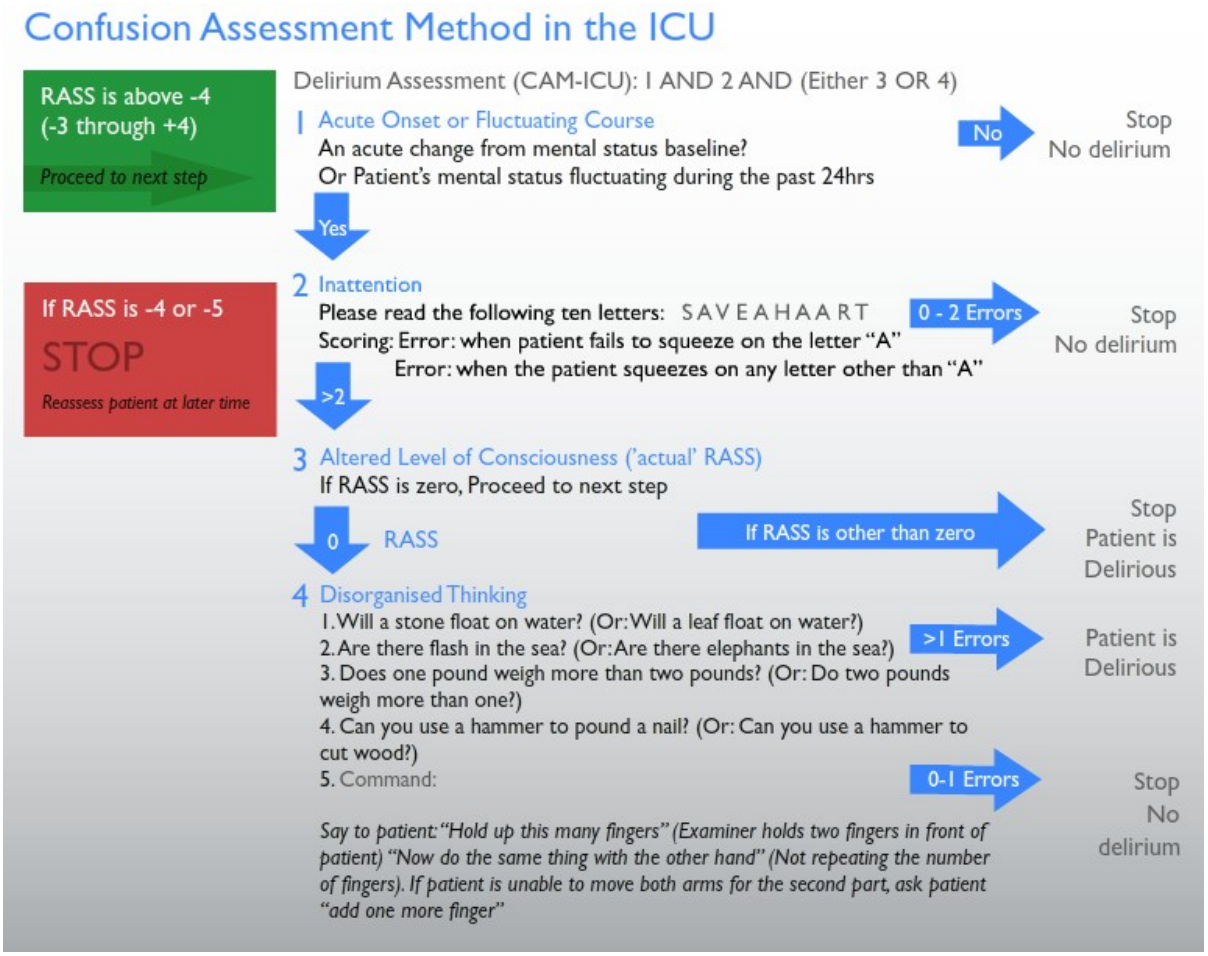
It is recommended that all ICU patients should be routinely monitored for delirium using a valid delirium screening tool at least once every nursing shift.

INSTRUMENTS TO MONITOR DELIRIUM

Several tools have been developed specifically for monitoring delirium in the ICU.

The Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) have the highest validity and reliability. The CAM-ICU can detect

delirium in 1-2 minutes in mechanically ventilated patients, and is usually linked to the RASS score to form a simultaneous assessment of sedation state and delirium status.



HOW TO TREAT DELIRIUM?

Treatment of delirium can be non-pharmacological or/and pharmacological.

Non-pharmacological treatments, such as noise reduction, natural light, regular reassurance and re-orientation, and sleep promotion lack evidence but are cheap and carry minimum risk. These should be used whenever possible.

There is little high quality evidence to guide the best drugs for treating delirium in ICU patients or which patients are most likely to benefit. All drugs used to treat delirium have potentially important side effects, so clinical judgement is important.

NON-PHARMACOLOGICAL TREATMENTS

Before you begin to treat delirium, it is important to recognise the predisposing factors that put a patient at risk of developing delirium. Such risk factors can include:

- Patient demographics (e.g. age and sex - older, male patients seem to be more at risk of delirium)
- Cognitive status (dementia, cognitive impairment, history of delirium, depression)
- Functional status (functional dependence, immobility, low level of activity, history of falls).

Having addressed these risk factors, you can think of **non-pharmacological** treatment first. Although there is lack of evidence on their effect, they are cheap interventions and carry minimum risk. These should be used whenever possible.
These can be:

- Noise reduction
- Ensure there is natural light coming in the ward
- Provide regular reassurance and re-orientation
- Promote natural sleep (see module 9)

EARLY MOBILIZATION WITH DELIRIUM

Early mobilization can reduce the incidence and duration of delirium.

(•) True

( ) False

Correct. A randomized controlled trial combining sedation reduction with early mobilisation in the ICU found that this approach reduced the incidence and duration of delirium, shortened ICU and hospital stay, and decreased hospital costs. Subsequent studies confirm the general benefits to patients from strategies that support early mobilisation, even during mechanical ventilation.

DRUGS USED TO TREAT DELIRIUM

Delirium is thought to result in abnormal communication within the brain, involving centres involved in arousal, attention, and cognition. Many different pathways and neurotransmitters are involved, including acetylcholine, serotonin, dopamine, GABA, and glutamate. The cause of delirium is incompletely understood.

There is little high quality evidence to guide the best drugs for treating delirium in ICU patients or which patients are most likely to benefit. All drugs used to treat delirium have potentially important side effects, so clinical judgement is important.

The drugs used to treat delirium are antipsychotics, because many of the features of delirium are similar to acute psychosis (for example agitation, hallucinations, and delusional thoughts). Antipsychotics act on multiple areas and pathways in the brain.

The *typical* or *first generation* antipsychotics include a large number of drugs. The commonest used to manage ICU delirium is **haloperidol.**

The *atypical* or *second generation* antipsychotics were developed more recently, and claimed to have less side effects. Several of these have been used to treat delirium in the ICU, including **olanzapine, quetiapine**, and **respiridone.** These drugs all have a range of potentially serious side effects. Some are mainly seen with chronic use (for example during treatment of schizophrenia or bipolar disorder), but other side effects are relevant to acute use during delirium management.

IMPORTANT SIDE-EFFECTS OF ANTIPSYCHOTIC DRUGS DURING CRITICAL ILLNESS

In most patients, antipsychotic drugs can be used safely in ICU and are effective for managing delirious patients with agitation and psychotic symptoms such as hallucinations and delusions. It is important to be aware of potential side effects, especially when higher doses are used for prolonged periods.

Some important side effects of antipsychotics are shown below:

QT ECG prolongation

All antipsychotic drugs can cause QT prolongation of the ECG. This can increase the risk of cardiac arrhythmias, and especially *torsade de pointes* which is a type of ventricular tachycardia. Torsades de pointes is often associated with hypotension, and can progress to ventricular fibrillation or sudden death. This complication is rare, but antipsychotic drugs should be used with caution in patients QT prolongation, a history of ventricular arrhythmias, or concomitant administration of other drugs which cause QT prolongation. It is advisable to measure the QTc on an ECG before using antipsychotics.

Sedation

Antipsychotics are all used to treat agitation, and have sedative properties. It is important to review the dose of antipsychotic drug in patients with decreased conscious level, particularly if other sedative drugs have been stopped.

Movement disorders

A recognised risk of all antipsychotic drugs is a range of movement disorders. Acutely, these can include dystonias (abnormal movements and spasms), muscle rigidity, and tremor. Any patient suffering abnormal movements or tone while receiving an antipsychotic drug should have this reviewed.

HALOPERIDOL

Haloperidol is widely used for first line management of ICU delirium.

- It can be administered intravenously, orally, and intramuscularly.
- After intravenous injection, onset of action is within 2-3 minutes. Clinical effects typically last 4-6 hours.

- Haloperidol has ≈20x higher concentration in brain tissue than plasma, which may explain the delayed offset of effects in some situations.
- Typical initial dose for agitated delirious ICU patients is 1-5 mg, repeated every 30-60 minutes until symptom control.
- Maintenance doses of 1-5mg every 4-6 hours can be used orally or intravenously.
- Doses >40 mg per 24 hours should be used with caution because of the risks of side effects.
- When high doses are used alternative atypical antipsychotics should be considered, such as olanzapine or quetiapine, which may have a lower risk of serious side effects.

PRACTICAL MANAGEMENT OF DELIRIUM

The evidence to guide the safest way of managing delirium is still limited.

Hypoactive delirium should not be routinely treated with antipsychotic drugs

The evidence supporting drug treatment for patients who are delirious (CAM-ICU positive) but not agitated is weak. As many antipsychotic drugs have important side effects they should be reserved for patients with agitated delirium.

Antipsychotic drugs may reduce the duration of delirium

There is some evidence that antipsychotic drugs may reduce the duration of delirium when used continuously following diagnosis. Based on current evidence it is logical to start a regular antipsychotic in a patient with agitated delirium and continue it until delirium has resolved.

Cholinesterase inhibitors should not be used to treat delirium in ICU patients

Cholinesterase inhibitors have been shown to have some benefit in treating delirium in elderly demented patients. A randomised trial of the cholinesterase inhibitor rivastigmine in delirious ICU patients was stopped early because more patients were dying in the treated group. This illustrates the fine balance between risk and benefit of using centrally acting drugs in the critically ill.

Dexmedetomidine is a potentially useful drug in ICU patients with delirium

Several large studies have compared the use of the $\alpha 2$ agonist dexmedetomidine (see module 3) for sedation compared with benzodiazepines or propofol. These trials suggest dexmedetomidine reduces the incidence and duration of delirium, especially compared to benzodiazepines. An exception is patients with benzodiazepine or alcohol withdrawal in whom benzodiazepines are the drugs of choice.

SUMMARY

Delirium is a common, poorly recognised complication of critical illness and is associated with higher mortality, longer ICU and hospital stay, and higher illness costs.

The key features of delirium are an *acute onset* of brain dysfunction with *fluctuation from the baseline state*. Patients suffer from *inattention*, *disordered thinking*, and *altered conscious level*, which can result in a range of symptoms including confusion, agitation, hallucinations, delusional thoughts, sleep deprivation, and coma.

Most patients with delirium have hypoactive delirium, which is easily missed. Less than10% of delirious patients are agitated. Screening patients routinely (once a shift) for delirium is necessary.

Management of delirium involves avoiding trigger agents, optimising the environment to help orientate the patient, and using antipsychotic drugs to manage agitation.