ACUTE CONFUSIONAL STATE WITH AND WITHOUT FEVER

Riadh Gouider, Alya Gharbi

30/10/23
14th RTC Africa
I have no conflict of interest, whether or not related to the content of this presentation.
Confusional state

A decompensation of cerebral function in response to one or more pathophysiological stressors

Most episodes lasting a few days but with episodes persisting for weeks or months in up to 20% of individuals
Confusional state

Before DSM-III

• Acute confusional state
• Encephalopathy
• Acute brain failure
• ICU psychosis
• Subacute befuddlement

DSM-III (1980)

Delirium

European Delirium Association BMC Medicine, 2014
Which term to use?

*Delirium versus encephalopathy versus an acute confusional state*

Expert consensus recommendation

- **Acute encephalopathy** → pathophysiologic state of the central nervous system “process,”
- **Delirium** → the symptoms observed at the bedside
- **Acute confusional state, acute brain dysfunction, acute brain failure, or altered mental status** → educational purposes
Overlap between hypoactive delirium and reduced arousal states (hyperactive delirium not included)
According to the DSM-5* classification, to be diagnosed with delirium a patient must display all of the following:

**Delirium**

- **Disturbance in attention**
  - Ask patient to name the months of the year backwards

- **Disturbance in awareness**
  - Ask patient their age, date of birth, place and current year

- **An additional disturbance**
  - Such as defect in:
    - Memory
    - Visuospatial ability
    - Language
    - Perception

- **Acute change**
  - Develops over a short period of time
  - Sudden change from baseline
  - Fluctuates during the course of a day
  - May require information from other staff, carers, or case notes

- **Evidence of cause**
  - Evidence that disturbance is a consequence of one or more of:
    - Another medical condition
    - Substance intoxication
    - Substance withdrawal
    - Exposure to a toxin

**No better explanation**

These disturbances are not better explained by a pre-existing, established or evolving neurocognitive disorder or coma state
Table 1 Comparing DSM classifications of delirium

<table>
<thead>
<tr>
<th>DSM-5</th>
<th>DSM-IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Disturbance in attention (i.e., reduced ability to direct, focus,</td>
<td>A. Disturbance of consciousness (i.e. reduced clarity of awareness of</td>
</tr>
<tr>
<td>sustain, and shift attention) and awareness (reduced orientation</td>
<td>the environment) with reduced ability to focus, sustain or shift</td>
</tr>
<tr>
<td>to the environment).</td>
<td>attention.</td>
</tr>
<tr>
<td>B. The disturbance develops over a short period of time (usually</td>
<td>B. A change in cognition or the development of a perceptual disturbance</td>
</tr>
<tr>
<td>hours to a few days), represents an acute change from baseline</td>
<td>that is not better accounted for by a pre-existing, established or</td>
</tr>
<tr>
<td>attention and awareness, and tends to fluctuate in severity during</td>
<td>evolving dementia.</td>
</tr>
<tr>
<td>the course of a day.</td>
<td>C. The disturbance develops over a short period of time (usually hours</td>
</tr>
<tr>
<td>C. An additional disturbance in cognition (e.g. memory deficit,</td>
<td>to days) and tends to fluctuate during the course of the day</td>
</tr>
<tr>
<td>disorientation, language, visuospatial ability, or perception).</td>
<td>D. There is evidence from the history, physical examination or</td>
</tr>
<tr>
<td>D. The disturbances in Criteria A and C are not better explained by</td>
<td>laboratory findings that the disturbance is caused by the direct</td>
</tr>
<tr>
<td>a pre-existing, established or evolving neurocognitive disorder and</td>
<td>physiological consequences of a general medical condition.</td>
</tr>
<tr>
<td>do not occur in the context of a severely reduced level of arousal</td>
<td></td>
</tr>
<tr>
<td>such as coma.</td>
<td></td>
</tr>
<tr>
<td>E. There is evidence from the history, physical examination or</td>
<td></td>
</tr>
<tr>
<td>laboratory findings that the disturbance is a direct physiological</td>
<td></td>
</tr>
<tr>
<td>consequence of another medical condition, substance intoxication</td>
<td></td>
</tr>
<tr>
<td>or withdrawal (i.e. due to a drug of abuse or to a medication), or</td>
<td></td>
</tr>
<tr>
<td>exposure to a toxin, or is due to multiple etiologies.</td>
<td></td>
</tr>
</tbody>
</table>


Changes in DSM-5 from DSM-IV shown in italics.
Delirium subtypes

**Hyperactive delirium**
- Predominantly restless and agitated
- Increased motor activity
- Loss of control of activity
- Restlessness
- Wandering

**Mixed motor type**
- Evidence of both subtypes in the previous 24 hours

**Hypoactive delirium**
- Predominantly drowsy and inactive
- Decreased activity
- Decreased action speed
- Decreased speed of speech
- Decreased amount of speech
- Listlessness
- Reduced awareness of surroundings
- Withdrawal

(Commonly mistaken for depression or dementia)

Christian Hosker, David Ward, BMJ 2017
## DSM-V: Delirium

- **A. Disturbance in attention** (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).

- **B.** The disturbance develops over a **short period of time (usually hours to a few days)**, represents an acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.

- **C. An additional disturbance in cognition** (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).

- **D.** The disturbances in Criteria A and C are **not better explained by a pre-existing**, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma.

- **E.** There is evidence from the history, physical examination or laboratory findings that the disturbance is a **direct physiological consequence of another medical condition, substance intoxication or withdrawal** (i.e. due to a drug of abuse or to a medication), or **exposure to a toxin**, or is due to **multiple etiologies**.
When should clinicians consider a diagnosis of confusional state?

- Any confused hospitalized patient and in high-risk patients with confusion in any setting

- When in doubt: it is always better to rule out delirium first than to attribute confusion to an underlying chronic disorder, such as dementia, and fail to recognize delirium

Melissa L.P. Mattison, MD, Annals of Internal Medicine, 2020
Confusional state in practice

In the emergency room:

1. Diagnostic of confusional state

2. Rule out differential diagnoses

3. Search for the underlying cause

- History – Examination
- History – Examination
- History – Examination +/- Clinical investigations
### Diagnosis: History

<table>
<thead>
<tr>
<th><strong>History</strong></th>
<th><strong>Diagnosis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Time course of the mental status or behavioral changes</td>
<td>New onset, fluctuating course suggestive of delirium; usually obtained from family member or caregiver rather than patient; patient may also have symptoms of depression or dementia, but an acute change should prompt an evaluation for potential delirium</td>
</tr>
<tr>
<td>Association of mental status changes with other events, including medication changes and development of physical symptoms</td>
<td>Obtained from review of the medical record or from a family member or caregiver</td>
</tr>
<tr>
<td>Medication history, including over-the-counter medications</td>
<td>Careful review of all medications taken, including pharmacy fill data and information from electronic health record to ensure an accurate list of medications is obtained</td>
</tr>
<tr>
<td>Sensory deprivation assessment</td>
<td>Absence of glasses or hearing aids normally worn by the patient</td>
</tr>
<tr>
<td>Pain assessment</td>
<td>Delirium has been associated with severe pain, especially in patients unable to effectively communicate; pain may be manifested only by agitation</td>
</tr>
</tbody>
</table>
## Common risk factors

### Predisposing conditions:
- Preexisting cognitive impairment
- Multiple comorbid conditions, including depression
- Polypharmacy
- Impaired sensation (e.g., vision, hearing)
- Impaired functional ability (i.e., activities of daily living diminished)
- History of alcohol misuse and/or malnutrition
- Anemia

### Precipitating factors:
- Severe illness (e.g., sepsis, stroke)
- Presence of tethers (e.g., urinary catheter) and/or physical restraints
- Surgery/anesthesia
- New psychoactive medication • Pain
- Environmental change
- Dehydration and/or electrolyte disturbances
- Urine retention/fecal impaction
Common risk factors

**Premorbid factors**
- Advanced age
- Dementia
- Low educational level
- High comorbidity burden
- Frailty
- Visual and hearing impairment
- Depression
- Alcohol abuse
- Poor nutrition
- Illicit drug, opioid or benzodiazepine use
- History of delirium

**Factors relating to presenting illness**
- Surgical stress
- Cardiovascular surgery
- Major abdominal surgery
- Aortic surgery
- Major joint surgery
- Emergency surgery
- Acute infections
- Dehydration
- Electrolyte imbalance
- Acute kidney injury
- Liver dysfunction
- Alcohol or drug withdrawal
- Seizures
- Heart failure
- Severity of illness
- Unplanned admission
- Medical admission
- Sepsis
- Failure of non-invasive ventilation
- Ventilation longer than 96 hours

**Post-admission factors**
- Pain
- Infection
- Invasive devices
- Immobility
- Metabolic abnormalities
- Prolonged ileus
- Blood transfusion
- All hospital and postoperative factors
- Opioids
- Polypharmacy
- Sleep deprivation
- Environmental factors
- Day–night disorientation or confusion
- Lack of communication with family
- Deep sedation
- Invasive devices
- Physical restraints
- Poor sleep
- Opioids
- Psychoactive drugs
- Benzodiazepines
- Anticholinergic agents
- Immobility
- Fall risk
- Longer duration of ventilation
- Infusions of benzodiazepines and opioids
- Physical restraints

[Jo Ellen Wilson, NATURE REVIEWS | DISEASE PRIMERS, 2020]
One key element:

- **Determining the timeline** of the mental status changes.

Other essential element:

Fluctuations in mental status:

- Patient seeming normal at times and very confused at others.

Melissa L.P. Mattison, MD, Annals of Internal Medicine, 2020, Geriatrics for specialists 2021
### Diagnosis: Examination

#### Physical Examination

| General medical examination, focusing on cardiac, pulmonary, and neurologic elements | Provides clues to causes of delirium; remember to look for transdermal patches |
| Cognition examination, including attention testing (see the Box: Commonly Used Tests of Attention) | Inattention is the hallmark cognitive deficit in delirium; patients with Lewy body dementia may have symptoms at baseline that are similar to dementia (behavioral disturbances, fluctuating course); even in these patients, an acute change should be evaluated and managed as delirium |

**One key element:**

→ Determining the level of consciousness and attention
Commonly Used Tests of Attention

- Digit span (up to 5 forward and 4 backward)
- Recite the days of the week and the months of the year in reverse order
- Continuous performance task (instruct patient to raise hand when he or she hears a certain letter in a list)
- Attention screening examination (show pictures; ask patient to remember and recall)
- Recite a list of serial 7's or 3’s
- Spell “world” backward
### Table 2 | Tools for the assessment of delirium

<table>
<thead>
<tr>
<th>Tool</th>
<th>Description</th>
<th>Reference</th>
</tr>
</thead>
</table>
| CAM                | Most widely used screening test for the presence of delirium; a four-item instrument based on DSM-III-R delirium criteria, requires the presence of acute onset and fluctuating course, inattention, and disorganized thinking or loss of consciousness                                                                 | Inouye et al. (1990)\(^{52}\)  
Wei et al. (2008)\(^{53}\) |
| CAM–ICU            | Delirium is diagnosed when patients demonstrate an acute change in mental status or fluctuating changes in mental status, inattention measured with either an auditory or a visual test, and either disorganized thinking or an altered level of consciousness. Importantly, the CAM–ICU can only be administered if the patient is arousable in response to a voice without the need for physical stimulation | Ely et al. (2001)\(^{113}\)  
Ely et al. (2001)\(^{114}\) |
| DRS-R98            | 16-item scale, including 13 severity items and 3 diagnostic items. Severity scores range from 0 to 39, with higher scores indicating more-severe delirium; delirium typically involves scores ≥15 points                                                                                   | Trzepacz et al. (2001)\(^{115}\) |
| DSI                | A structured interview detects the presence or absence of seven DSM-III criteria for delirium; delirium is said to be present if disorientation, perceptual disturbance or disturbance of consciousness have presented within the past 24 h                                                                 | Albert et al. (1992)\(^{116}\) |
| MDAS               | Measures delirium severity on a 10-item, four-point observer-rated scale with scores that range from 0 to 30                                                                                     | Breitbart et al. (1997)\(^{54}\) |
| NEECHAM Confusion Scale | Nine scaled items divided into three subscales: subscale I, information processing (score range 0–14 points), evaluates components of cognitive status; subscale II, behavior (score range 0–10 points), evaluates observed behavior and performance ability; subscale III, performance (score range 0–16 points), assesses vital function (that is, vital signs, oxygen saturation level and urinary incontinence). Total scores can range from 0 (minimal function) to 30 (normal function). Delirium is present if the score is ≤24 points | Neelon et al. (1996)\(^{117}\) |
| ICDSC              | Bedside screening tool for delirium in the intensive care unit setting; eight-item checklist based on DSM-IV\(^{®}\) criteria, items scored as 1 (present) or 0 (absent); a score ≥4 points indicates delirium                                                                 | Bergeron et al. (2001)\(^{118}\) |
| Cognitive Test for Delirium | Can be used with patients unable to speak or write; assesses orientation, attention, memory, comprehension and vigilance, primarily with visual and auditory modalities. Each individual domain is scored 0–6 in two-point increments, except for comprehension, which is scored in single-point increments. Total scores range from 0 to 30, with higher scores indicating better cognitive function | Hart et al. (1997)\(^{119}\)  
Hart et al. (1996)\(^{120}\) |

Abbreviations: CAM, Confusion Assessment Method; CAM–ICU, Confusion Assessment Method–Intensive Care Unit; DRS-R98, Delirium Rating Scale; DSI, Delirium Symptom Interview; DSM, Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, Arlington, VA); ICDSC, Intensive Care Delirium Screening Checklist; MDAS, Memorial Delirium Assessment Scale.
# Differential Diagnosis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Delirium</th>
<th>Alzheimer disease</th>
<th>Psychotic disorders</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descriptive features</td>
<td>Confusion and inattention</td>
<td>Memory loss</td>
<td>Loss of contact with reality</td>
<td>Sadness, anhedonia</td>
</tr>
<tr>
<td>Onset</td>
<td>Acute</td>
<td>Insidious</td>
<td>Acute or slow</td>
<td>Slow</td>
</tr>
<tr>
<td>Course</td>
<td>Fluctuating, often worse at night</td>
<td>Chronic, progressive (but stable over the course of a day)</td>
<td>Chronic, with exacerbations</td>
<td>Single or recurrent episodes; can be chronic</td>
</tr>
<tr>
<td>Duration</td>
<td>Hours to months</td>
<td>Months to years</td>
<td>Months to years</td>
<td>Weeks to months</td>
</tr>
<tr>
<td>Consciousness</td>
<td>Altered</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Attention</td>
<td>Impaired</td>
<td>Normal, except in late stages</td>
<td>May be impaired</td>
<td>May be impaired</td>
</tr>
<tr>
<td>Orientation</td>
<td>Fluctuates</td>
<td>Poor</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Speech</td>
<td>Incoherent</td>
<td>Mild errors</td>
<td>Normal or pressured</td>
<td>Normal or slow</td>
</tr>
<tr>
<td>Thought</td>
<td>Disorganized</td>
<td>Impoverished</td>
<td>Disorganized</td>
<td>Normal</td>
</tr>
<tr>
<td>Illusions and hallucinations</td>
<td>Common (often visual)</td>
<td>Rare, except in late stages</td>
<td>Common</td>
<td>Not usually</td>
</tr>
<tr>
<td>Perceptions</td>
<td>Altered</td>
<td>Altered or normal</td>
<td>Altered</td>
<td>Normal</td>
</tr>
<tr>
<td>Psychomotor changes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Reversibility</td>
<td>Usually</td>
<td>Rarely</td>
<td>Rarely</td>
<td>Possibly</td>
</tr>
<tr>
<td>EEG reading</td>
<td>Moderate to severe background slowing</td>
<td>Normal or mild diffuse slowing</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>
Confusional state in practice

In the emergency room:

1. Diagnostic of confusional state
2. Rule out differential diagnoses
3. Search for the underlying cause

Take patient’s temperature

Confusional state with fever
Confusional without fever
Confusional state in practice

Etiology

Confusional state without fever
1. Toxic, iatrogenic
2. Epilepsy
3. Metabolic
4. Vascular:
   SDH, Stroke
5. Prion disease
6. Auto-immune encephalitis
7. Degenerative diseases: DLB

Confusional state with fever
1. CNS infections: E.g.
   Neurological complications of Malaria
   Herpes, West Nile
   MIS-C Post SARS-CoV-2
2. Neuroleptic malignant syndrome
3. An infection outside the CNS in a patient with a brain disease (e.g., dementia)
Confusional state in practice

Etiology

Confusional state with fever

1. CNS infections: E.g.
   - Neurological complications of Malaria
   - Herpes, West Nile
   - MIS-C Post SARS-CoV-2
2. Neuroleptic malignant syndrome
3. An infection outside the CNS in a patient with a brain disease (e.g., dementia)

- Laboratory assessment: CBC, C-reactive protein, +/- CK
- CT scan or brain MRI
- Lumbur puncture
- Other infectious work-up: Chest radiography, urinalysis, culture
Confusional state in practice

Etiology

- Toxic, iatrogenic
- Epilepsy
- Metabolic
- Vascular: SDH, Stroke
- Prion disease
- Auto-immune encephalitis
- Degenerative diseases: DLB

Confusional without fever

- History
- Examination
- Basic laboratory tests (CBC, iono, liver)
- EEG
- CT Scan, Brain MRI
- Anti-neurone antibodies
- CSF analysis (Anti-neuronal Ab, CSF Ig)
# Confusional state in practice

1. **History**
2. **Examination**
3. **Clinical investigations**

<table>
<thead>
<tr>
<th><strong>Targeted laboratory evaluation</strong> ( (selected \text{ tests based on clues from history and physical}) )</th>
<th><strong>Based on history and physical examination, consider:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Laboratory tests: CBC, electrolytes, calcium, glucose, renal function, liver function, thyroid function, urinalysis, cultures of urine, blood, sputum, drug levels, toxicology screen, ammonia level, vitamin B12 level, cortisol level</td>
</tr>
<tr>
<td></td>
<td>• Arterial blood gas</td>
</tr>
<tr>
<td></td>
<td>• Electrocardiography</td>
</tr>
<tr>
<td></td>
<td>• Chest X-ray</td>
</tr>
<tr>
<td></td>
<td>• Lumbar puncture reserved for evaluation of fever with headache, and meningeal signs, or suspicion of encephalitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Targeted neuroimaging</strong> ( (selected \text{ patients}) )</th>
<th><strong>Targeted neuroimaging</strong> ( (selected \text{ patients}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Assess focal neurological changes, since stroke can present as delirium</td>
</tr>
<tr>
<td></td>
<td>• Suspicion of encephalitis for temporal lobe changes</td>
</tr>
<tr>
<td></td>
<td>• History or signs of head trauma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Electroencephalography</strong> ( (selected \text{ patients}) )</th>
<th><strong>Electroencephalography</strong> ( (selected \text{ patients}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Evaluate for occult seizures</td>
</tr>
<tr>
<td></td>
<td>• Differentiate psychiatric condition from delirium</td>
</tr>
</tbody>
</table>

*Inouye et al. Lancet. 2014*
Case 1

Mrs, 49 yo

- A woman aged 49 years old
- from Congo
- 3 months after a malarial attack: alteration of consciousness + generalized epileptic seizure
- Laboratory tests: hepatic cytolysis and leukolymphopenia
- Normal brain CT scan
Case 1

Mrs, 49 yo

- Smear examination -> severe malarial attack
Neurological complications of Malaria

Cerebral malaria

Additional neurological manifestations:

- Posterior reversible encephalopathy syndrome (PRES) reversible cerebral Vasoconstriction syndrome (RCVS)
- Malarial retinopathy
- Post-malarial neurological syndrome (PMNS)
- Acute disseminated encephalomyelitis (ADEM)
- Guillain-Barré syndrome (GBS)
- Cerebellar ataxia

Survivors of severe malaria

Neurological sequelae

- Motor deficits
- Ataxia
- Paresis
- Movement disorders
- Seizure
- Visual impairments
- Hearing impairments
- Speech or language impairments
- Development delay

Cognitive deficits

- Attention deficits
- Learning difficulties
- Cognitive ability deficits (fine motor, visual reception, receptive and expressive language)
- Memory deficits
- Non-verbal function deficits

Behavioral alterations

- Emotional reactions
- Disruptive behaviors
- Attention deficit and hyperactivity disorders
- Conduct disorders
- Oppositional defiant disorders
- Sleep problems
- Anxiety

Trivedi, S, Chakravarty, Curr Neurol Neurosci Rep (2022)
Case 2

Mrs FDA, 78 yo

- Medical history: high blood pressure, dyslipidemia, thyroid disorder
- Parkinson's disease stable for 3 years on Modopar 250, melatonin, paroxetine
- **Worsening of motor symptoms** in May 2023: started on amantadine 200 mg/day, leading to the emergence of psychobehavioral disturbances, followed by amitriptyline
- **Worsening symptoms**: visual hallucinations, impaired vigilance, sleep disturbances
- Fell and fractured the femoral neck
- Paroxysmal episode of abnormal movements and screams, followed by generalized hypotonia and gradual awakening → *Levetiracetam 125 mg/day* *(received 750 mg/day)*
Case 2  Mrs FDA, 78 yo

Neurological examination:

• Somnolent, Glasgow Coma Scale (GCS) score = 13

• Temporo-spatial disorientation

• Parkinsonian syndrome Blood tests: CBC, C-reactive protein, ionogram, transaminases, and thyroid-stimulating hormone were all within normal limits.

• Normal brain MRI

EEG: Triphasic waves, delta slowing
Toxic/iatrogenic causes of confusional state

- **Alcoholism**: alcoholic intoxication, alcoholic hallucinosis, delirium tremens, abrupt withdrawal

- **Psychoactive substances**: cannabis; high-dose ether, solvents, hallucinogens, amphetamines, barbiturates, opioids

- **Occupational or accidental poisoning**: carbon monoxide, lead, arsenic

- **Medication poisoning** (especially in the elderly), antidepressants, anticholinergics, benzodiazepines, lithium, corticosteroids, antibiotics.
### Table 2. Drugs That May Cause Delirium and Potential Substitutes*

<table>
<thead>
<tr>
<th>Agent</th>
<th>Potential Mechanism Leading to Delirium</th>
<th>Potential Substitute</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines (long- and short-acting)</td>
<td>CNS sedation</td>
<td>Nonpharmacologic sleep management; if required for patient safety, use short-acting in smallest effective dose</td>
<td>May be required for sedation in critical care setting; associated with precipitation of or worsening delirium</td>
</tr>
<tr>
<td>Alcohol</td>
<td>CNS sedation</td>
<td>If history of regular/significant intake, consider withdrawal syndrome and treat appropriately</td>
<td>-</td>
</tr>
<tr>
<td>Antidepressants (the tertiary amine tricyclic agents: amitriptyline, imipramine, doxepin)</td>
<td>Anticholinergic toxicity</td>
<td>Should be reserved for patients who do not respond to first-line treatment with SSRIs or SNRIs</td>
<td>-</td>
</tr>
<tr>
<td>Antihistamines, especially first-generation (e.g., diphenhydramine)</td>
<td>Anticholinergic toxicity</td>
<td>Nonpharmacologic sleep protocol; alternative decongestant strategies</td>
<td>Often included in over-the-counter preparations for sleep</td>
</tr>
<tr>
<td>Anticholinergics: bladder antispasmodics</td>
<td>Anticholinergic toxicity</td>
<td>Consider behavioral interventions</td>
<td>Newer agents may have fewer CNS adverse effects</td>
</tr>
<tr>
<td>Opioid analgesics</td>
<td>Anticholinergic toxicity, CNS sedation, constipation</td>
<td>Opiate-sparing analgesic regimens; use the lowest effective dose (opioid metabolites can accumulate in renal impairment) and provide supportive measures (e.g., to prevent constipation)</td>
<td>-</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Anticholinergic toxicity, CNS sedation</td>
<td>Avoid use altogether; if use is necessary for patient safety and care delivery, use lowest effective dose</td>
<td>Discuss risks and potential benefits with patient or surrogate decision maker</td>
</tr>
<tr>
<td>Antibiotics, especially fluoroquinolones</td>
<td>GABA and NMDA receptor effects</td>
<td>Choose alternative antimicrobial agent when possible</td>
<td>Can also be associated with hypoglycemia, which may worsen delirium</td>
</tr>
</tbody>
</table>

*Melissa L.P. Mattison, MD, Annals of Internal Medicine 2020*
Case 3

Mr, 78 yo

- 67-year-old man, a farmer,

- Medical history: ?

- Brought to the emergency room after an evening. He was:
  
  - Disoriented in time and space
  
  - Calm, perplexed, slowed down
  
  - Without neurological signs of localization or fever

→ Diagnosis?
• Brother's interview:

The patient has been taking Depakine for a week due to epilepsy.

• Diagnosis?

1. Postictal confusion
2. Non-convulsive status epilepticus
3. Drug/toxic encephalopathy
Case 3

Mr, 78 yo

State of non-convulsive status.
Case 4

Mr BF, 75 yo

• Medical history: Lung cancer /chemotherapy

• 5 months ago: rapid onset of behavioral disturbances

• Neurological examination:
  - Confusion
  - Pyramidal syndrome
  - Cerebellar syndrome
Case 4

Mr BF, 75 yo

Chronic subdural hematoma
Key Recommendations of the NICE Guideline for Delirium

- Assess delirium risk factors when patients are admitted to the hospital, especially those aged ≥65 years, those with cognitive impairment, those with a current hip fracture, and those with severe illness.
- Prevent delirium by addressing risk factors using a tailored multicomponent intervention.
- Screen for incident delirium by assessing recent changes or fluctuations in cognitive function, perception, physical function, and social behavior on admission and at least daily thereafter.
- Diagnose delirium using a clinical assessment based on formal criteria and conducted by a trained health care professional; document in the medical record.
- Manage delirium by:
  - Identifying and managing possible causes
  - Ensuring effective communication and reorientation and providing reassurance
  - Considering the involvement of family, friends, and caregivers
  - Providing care in a suitable environment

If a person with delirium is distressed or is a risk to themselves or others:
- Use verbal and nonverbal deescalation techniques, such as quietly sitting at the bedside and engaging the patient in conversation or playing relaxing music.
- If these are not effective or appropriate, consider short-term (usually ≤1 week) haloperidol at the lowest clinically appropriate dose and titrate cautiously according to symptoms.
- Avoid using antipsychotic drugs if possible in patients with Parkinson disease or Lewy body dementia.
Management

• Symptomatic treatment
  - *Nonpharmacological acute treatment strategies*: first-line treatments for all patients. It include reorientation and behavioral intervention

  - *Pharmacological therapy*
    • Antipsychotics (neuroleptics)
    • Benzodiazepines
    • Trazodone

• Etiological treatment
## Management

### Table 3 | Pharmacological therapy for delirium

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Adverse effects</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td><strong>Acute therapy</strong></td>
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<tr>
<td><strong>Antipsychotics</strong></td>
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<tr>
<td>Haloperidol</td>
<td>0.5–1 mg PO or IM; can</td>
<td>Extrapyramidal syndrome, prolonged QT interval</td>
<td>Randomized, controlled trials demonstrate reduction in symptom severity and duration¹,²</td>
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<tr>
<td></td>
<td>repeat every 4 h (PO) or</td>
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<tr>
<td></td>
<td>every 60 min (IM)</td>
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<tr>
<td><strong>Atypical antipsychotics</strong></td>
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<tr>
<td>Risperidone</td>
<td>0.5 mg BID</td>
<td>Extrapyramidal syndrome, prolonged QT interval</td>
<td>Randomized, controlled trials comparing efficacy against haloperidol showed comparable response rates³,⁴</td>
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<tr>
<td>Olanzapine</td>
<td>2.5–5 mg daily</td>
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<tr>
<td>Quetiapine</td>
<td>25 mg BID</td>
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<tr>
<td><strong>Benzodiazepines</strong></td>
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<tr>
<td>Lorazepam</td>
<td>0.5–1 mg PO; can</td>
<td>Paradoxical excitation, respiratory depression, excess</td>
<td>Did not show improvement in condition; treatment limited by adverse effects³¹</td>
</tr>
<tr>
<td></td>
<td>repeat every 4 h</td>
<td>ive sedation, confusion</td>
<td></td>
</tr>
<tr>
<td><strong>Cholinesterase inhibitors</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Donepezil</td>
<td>5 mg QD</td>
<td>Nausea, vomiting, diarrhea</td>
<td>No randomized, controlled studies have been conducted; some case studies have indicated promise³⁵,³⁶</td>
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<tr>
<td><strong>Propylactic therapies (potential)</strong></td>
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<td></td>
<td></td>
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<tr>
<td><strong>Antipsychotics</strong></td>
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</tr>
<tr>
<td>Haloperidol</td>
<td>0.5–1 mg PO or IM; can</td>
<td>Extrapyramidal syndrome, prolonged QT interval</td>
<td>Use in surgical cases may reduce delirium incidence; needs to be confirmed in additional studies³⁷,³⁸</td>
</tr>
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<td></td>
<td>repeat every 4 h (PO) or</td>
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<td>Donepezil</td>
<td>5 mg QD</td>
<td>Nausea, vomiting, diarrhea</td>
<td>Prevention studies have not demonstrated efficacy³¹,³²</td>
</tr>
</tbody>
</table>

¹Antipsychotics are the most widely used drugs for the treatment of delirium-related agitation but can have marked adverse effects. ²Benzodiazepines should be reserved for treatment of drug withdrawal, diffuse Lewy body disease, or as second-line treatment following failure of antipsychotics. ³Not currently accepted clinical therapies. Abbreviations: BID, twice daily; IM, Intramuscularly; PO, per os (by mouth); QD, once daily.
# Prevention of delirium

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Recommendations for the prevention of delirium</th>
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<tbody>
<tr>
<td><strong>Prevention of delirium</strong></td>
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<tr>
<td>Avoid causal factors: unnecessary hospitalization, polypharmacy</td>
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<td>Timely recognition of prodromal symptoms: agitation, vivid dreams, insomnia, hallucinations</td>
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<td>If inpatient admission is necessary, the patient should receive qualified geriatric care right from the start, i.e., in perioperative management</td>
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<td>Dementia patients should be offered constant accompaniment by their family or other close caregivers (“sitters”)</td>
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<tr>
<td>Consistent delirium screening, assessment of dementia, depression, anxiety disorders, addictive disorders (alcohol, benzodiazepines, nicotine), identification of history of delirium, geriatric consultation, and medication review are recommended</td>
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<tr>
<td>Minimizing stress, giving time for questions, and optimal pain management are also recommended for the perioperative setting</td>
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</table>
Key messages

- Confusional state ≃ Delirium
- Diagnostic: History and Examination
- Search for Risk factors
- Investigations: with and without fever
- Management: symptomatic and etiological