Delirium is a complex neuropsychiatric syndrome with an acute onset and fluctuating course; it is common in all medical settings. Delirium occurs in about 15-20% of all general admissions to hospital; it occurs with higher frequency in elderly people and in those with pre-existing cognitive impairment. Delirium has many synonyms, reflecting its ubiquitous nature rather than distinct conditions. These synonyms include acute brain failure, acute confusional state, and post-operative psychosis. Delirium has not been well studied owing to methodological difficulties and a lack of consensus about its definition. Thus, delirium has been underappreciated as an independent entity that requires therapeutic intervention beyond identification of the syndrome and amelioration of the underlying cause. The development of a clearer definition, improved detection and assessment tools, and recognition of the significant independent morbidity associated with delirium have substantially changed this situation. These developments coupled with a greater awareness of the needs of an increasingly large population of elderly people make a review of the day to day management of patients with delirium timely.

Methods
This review is based on the results of a Medline search for articles published between 1980 and 1999 using the key words “delirium,” “acute confusion,” “management,” and “treatment”; as well as hand searching for articles in major journals in general and old age medicine and psychiatry published during the past five years; inspection of recent treatment guidelines published by the American Psychiatric Association; and a review of references cited within these sources. Because of variability in the methodological quality of research into delirium, articles were selected for inclusion on the basis of an appraisal of the usefulness and validity of the studies.

Clinical features
The symptoms of delirium are wide ranging, and although they are non-specific, their fluctuating nature is highly characteristic and is a valuable diagnostic indicator. The core disturbance involves an acute generalised impairment of cognitive function that affects orientation, attention, memory, and planning and organisational skills. Other disturbances, such as those of the sleep-wake cycle, thought processes, affect, perception, and activity levels, are underemphasised in diagnostic systems but contribute substantially to problems in identifying and managing delirium. Depending on which symptoms are apparent, delirium may be mistaken for a variety of disorders including dementia, mood disorders, and functional psychoses.

Identification
Delirium is underidentified in clinical practice; non-detection rates of 33-66% are typically reported. The agitated, disturbed image of delirium tremens is an inaccurate and damaging stereotype because it represents the minority of cases, and the existence of this stereotype is linked to the underdetection of somnolent or hypoactive cases. Failure to diagnose the disorder does not merely reflect preferences in terminology but represents an actual failure to recognise and treat the disorder appropriately and is associated with a poorer outcome. Detection can be improved by implementing educational programmes and by putting greater emphasis on routine cognitive testing and the use of screening instruments. The Confusion

Summary points
- Delirium is especially common in elderly patients and poses a substantial challenge for clinicians.
- Delirium comprises a wide range of symptoms, but the prevailing narrow definition impedes diagnosis and efforts to improve treatment.
- Diagnosis can be improved by clinicians becoming more aware of hypofrontal presentations, incorporating cognitive assessment into routine practice, and using simple screening instruments.
- Environmental strategies for treatment are free of adverse effects but are underutilised.
- Neuroleptics (such as haloperidol) continue to be used as first line treatment, but benzodiazepines are indicated in specific situations.
Risk factors and causes

The causes of delirium are many. In a typical case, predisposing and precipitating factors interact with multiple aggravating or perpetuating factors, which influence the course. The multifactorial nature is often underemphasised, but studies that have accounted for the possibility of multiple causes have found that between two and six factors may be present in any single case. It is therefore vital to be aware of risk factors and, having identified an explanation for delirium, remain vigilant as to the possibility of additional factors. Attempting to identify and treat a single cause is overly simplistic: each case needs detailed, repeated assessment for multiple potential factors.

Delirium is caused by factors in the patient as well as by pharmacological and environmental factors (box). Age, pre-existing cognitive impairment, severe comorbidity, and exposure to medication are robust predictors of the risk of delirium. Models of causation that quantify the role of predisposing factors and precipitating insults have shown that cumulative interactions with the baseline risk are especially predictive. If vulnerability at baseline is low, patients are resistant to delirium despite exposure to significant precipitating factors, but if vulnerability at baseline is high, delirium is likely to occur with exposure to only minor precipitating factors.

Although many risks for delirium reflect the enduring characteristics of the patient, some factors can be modified to prevent onset. At the very least, patients at high risk warrant close observation for emergent delirium and prompt intervention. Medications are implicated in 20-40% of cases: most...
prescribed drugs can cause delirium but benzodi-
azepines, narcotics, and drugs with anticholinergic
activity have a particular propensity. Many drugs and
their metabolites may unexpectedly contribute to caus-
ing delirium because their anticholinergic effects are
unrecognised. This was illustrated by a study that iden-
tified sufficient anticholinergic activity to cause signifi-
cant impairments in memory and attention in elderly
patients; this activity occurred in 10 of the 25 drugs
most commonly prescribed to elderly people including
theophylline, digoxin, and warfarin. It is therefore
prudent to minimise exposure to drugs and to reduce
doses or stop administration of high risk compounds
especially during high risk periods, such as the perioperative period. Many risk factors may simply be
markers of general morbidity, and studies showing the
preventive impact of modification of these risk factors
are lacking but important. None the less, preliminary
evidence indicates that interventions that reduce
sensory deficits, immobility, sleep disturbance, dehy-
dration, and cognitive impairment can reduce the
number of episodes of delirium and their duration.

Treating patients with delirium

Although delirium indicates the existence of an under-
lying pathology, it has significant independent morbid-
ity; patients with delirium require longer hospitalisa-
tion than control patients without delirium; and there
is a high frequency of complications (such as falls,
infections, and pressure sores) in patients with
delirium. Additionally, patients with delirium are more
likely to subsequently need care in an institution. The
negative impact of delirium may also include an
increased risk of death. Treatment should be aimed at
the specific symptoms of delirium, and efforts should
be made to identify and treat underlying causes. Diag-
nosis and treatment occur concurrently, and regular
evaluation of progress is important. Because of its seri-
ous nature, an episode of delirium is often best
managed in hospital because aggressive investigation
and treatment can be facilitated; however, this
advantage must be balanced against the potentially
deleterious effects on elderly people or those who have
cognitive impairment of a sudden change in envi-
ronment. In the United Kingdom patients with delirium
may give informed consent during lucid periods, but in
patients deemed incompetent urgent interventions are
governed by common law doctrine—that is, treatment
may be given without informed consent if medical col-
leagues would generally consider it appropriate and a
reasonable person would want it. The competitive ben-
zodiazepine antagonist flumazenil has been used to
temporarily restore mental capacity in patients with
delirium and hepatic failure to allow them to
participate in decisions about treatment or personal
affairs.

During the postoperative period patients are at
high risk for delirium, but delirium occurring at this
time is particularly amenable to therapeutic efforts. A
large, prospective, multicentre study directly implicated
surgery and anaesthesia as factors contributing to the
development of both short term and long term
postoperative cognitive impairment, but there
remains uncertainty about the specific factors that con-
tribute to delirium (such as the type and duration of
procedure, the circumstances of the operation, and the
pharmacological agents used) (box). Nevertheless,
系统atic strategies to detect and manage the
condition, which involve providing preoperative
psychological support (education and reduction of
anxiety), the use of patient controlled analgesia, and
careful postoperative management, have significant
benefits over traditional reactive care and can reduce
the incidence of delirium.

Environmental factors in treating delirium

Providing support and orientation
Communicate clearly and concisely; give repeated verbal reminders of the
day, time, location, and identity of key individuals, such as members of the
treatment team and relatives
Provide clear signposts to patient’s location including a clock, calendar,
chart with the day’s schedule
Have familiar objects from the patient’s home in the room
Ensure consistency in staff (for example, a key nurse)
Use television or radio for relaxation and to help the patient maintain
contact with the outside world
Involves family and caregivers to encourage feelings of security and
orientation

Providing an unambiguous environment
Simplify care area by removing unnecessary objects; allow adequate space
between beds
Consider using single rooms to aid rest and avoid extremes of sensory
experience
Avoid using medical jargon in patient’s presence because it may encourage
paranoia
Ensure that lighting is adequate; provide a 40-60 W night light to reduce
misperceptions
Control sources of excess noise (such as staff, equipment, visitors); aim for
< 45 decibels in the day and < 20 decibels at night
Keep room temperature between 21.1°C to 23.8°C

Maintaining competence
Identify and correct sensory impairments; ensure patients have their glasses,
hearing aid, dentures. Consider whether interpreter is needed
Encourage self care and participation in treatment (for example, have
patient give feedback on pain)
Arrange treatments to allow maximum periods of uninterrupted sleep
Maintain activity levels; ambulatory patients should walk three times each
day; non-ambulatory patients should undergo a full range of movements
for 15 minutes three times each day.
Environmental strategies are free from adverse effects, but they are underutilised and are often applied only in response to behavioural disturbance rather than in response to the degree of cognitive impairment. The fact that these strategies are most commonly used in hyperactive patients may reflect the prevailing idea that “severe” delirium is associated with hyperactive, disturbed patients; the reality is that these patients have better outcomes than patients who are underactive and less disturbed. It remains unclear whether better outcomes in hyperactive patients reflect underlying causes that are more treatable or differences in treatment.

Family members or caregivers can answer questions about what a patient’s mental status was before illness and facilitate efforts to reassure and reorient patients. Explaining delirium to family members is important because caregivers who are upset or ill informed can exacerbate a patient’s distress. Delirium may herald the terminal stages of illness, and it can shape enduring memories of loved ones as “crazy” or disturbed unless it is explained and managed sensitively. Because symptoms of delirium are often not fully resolved at the time the patient is discharged from hospital, relatives frequently play crucial roles in planning and monitoring care.

Drug treatment

Drug treatment of delirium requires careful consideration of the balance between the effective management of symptoms and potential adverse effects. Prescribing is often influenced by pressure from relatives, time constraints, or difficulties in communication between medical and nursing staff. The use of psychotropic drugs complicates the ongoing assessment of mental status, can impair the patient’s ability to understand or cooperate with treatment, and is associated with a greater incidence of falls. It is therefore important to clarify the reasons for using drugs to treat delirium: is the primary aim to alleviate delirium or to contain problem behaviour? Sedative compounds can improve agitation but may worsen cognitive impairment. A minority of patients require sedation to protect themselves. Less medication is required in cases in which delirium is identified early by screening, but there is a lack of studies of the effectiveness of pharmacological prophylaxis in high risk populations.

Antipsychotic drugs

Antipsychotics are the cornerstone of pharmacological treatment. Neuroleptics ameliorate a range of symptoms, are effective both in patients with a hyperactive or hypoactive clinical profile, and generally improve cognition. The onset of their action is rapid: improvement is usually evident within hours or days and thus occurs before underlying causes are treated. Neuroleptics are superior to benzodiazepines in treating delirium that has been caused by factors other than alcohol withdrawal or sedative hypnotics. Chlorpromazine, droperidol, and haloperidol have similar efficacy, but haloperidol is preferred because it has fewer active metabolites, limited anticholinergic effects, less sedative and hypotensive effects, and can be administered by different routes. Although the use of high potency antipsychotic drugs like haloperidol brings an increased risk of extrapyramidal side effects, the actual reported incidence is low. Moreover, intravenous administration of haloperidol seems to be less likely to cause extrapyramidal side effects in patients with delirium. Droperidol is more suitable when a faster onset of action or greater sedation is required. Pimozide is a potent calcium antagonist and may be more appropriate for treating delirium that is accompanied by hypercalcaemia.

The dose of an antipsychotic drug is determined by the route of administration, the patient’s age, the amount of agitation, the patient’s risk of developing side effects, and the therapeutic setting. Low dose oral haloperidol (1 mg to 10 mg/day) improves symptoms in most patients. Information on drug treatment in highly disturbed patients comes from studies of patients with general agitation rather than patients with delirium. A clear association between the successful control of agitation and an improved outcome in delirium has not been shown but it can be inferred from evidence linking poorer outcomes to the complications of untreated illness, such as non-compliance with treatment (for example, refusing medication) and immobility. A treatment regimen for severe cases requiring prompt, aggressive control of symptoms is outlined in the box.

<table>
<thead>
<tr>
<th>Pharmacological treatment of severe disturbance in delirium</th>
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<tbody>
<tr>
<td>• Administer 0.5–10 mg haloperidol (intramuscularly or intravenously) depending on level of disturbance and likely tolerance (having considered age, physical status, and risk of side effects)</td>
</tr>
<tr>
<td>• Observe patient for 20–30 minutes. If the patient remains unmanageable but has not had any adverse effects, double the dose and continue monitoring:</td>
</tr>
<tr>
<td>• Repeat the cycle until an acceptable response occurs or side effects occur</td>
</tr>
<tr>
<td>• Upper limits on doses have not been clearly established, but up to 100 mg of intravenous haloperidol every 24 hours is generally safe as is up to 60 mg intravenous haloperidol every 24 hours if benzodiazepines are used concomitantly</td>
</tr>
</tbody>
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Benzodiazepines

Benzodiazepines are first line treatment for delirium that is associated with seizures or withdrawal from alcohol or sedatives. They are also a useful adjunctive treatment for patients who cannot tolerate antipsychotic drugs because lower doses can be used and their effects can be rapidly reversed with flumazenil. The therapeutic aims of drug treatment should be explicit since anxiolytic, sedative, and hypnotic effects
occur as doses are increased. Benzodiazepines can both protect against delirium and be a risk factor for it; this highlights the need for judicious use in patients dependent on alcohol or benzodiazepines. Lorazepam has several advantages owing to its sedative properties, rapid onset, and short duration of action; it also has a low risk of accumulation; there are no major active metabolites; and its bioavailability is more predictable when it is given intramuscularly. Lower doses are necessary in elderly patients, those with hepatic disease, or those receiving compounds that undergo extensive hepatic oxidative metabolism (for example, cinemidine and isoniazid). The recommended upper limits for intravenous lorazepam are 2 mg every four hours.\(^1\) Giving adequate initial doses reduces the risk of paradoxical excitement (that is, disinhibition with worsening of behavioural disturbance).

**Emerging therapies**

Disturbances of cholinergic metabolism are implicated in cases in which delirium is caused by hypoxia, traumatic brain injury, or hypoglycaemia, or is drug related. Anticholinergic delirium is generally treated conservatively by withdrawing the offending agent and occasionally by administering physostigmine.\(^2\) Other procholinergic agents used to counter cholinergic deficits in dementia have theoretical potential but are not recommended owing to the risk of causing adverse effects. Current smoking has been identified as a possible protective factor against delirium,\(^3\) but the usefulness of nicotine replacement treatment in protecting against delirium has not been tested.

Trazadone and mianserin are antidepressant compounds that share antagonistic actions at 5-HT\(_2\) (serotonin) receptors. Open studies of low dose treatment of delirium with these compounds have found a rapid reduction of non-cognitive symptoms in particular. This effect was independent of the mood altering actions of the drugs.\(^4\)\(^5\)\(^6\) Other reports have advocated the use of light therapy,\(^7\) but the usefulness of this treatment needs to be more fully evaluated before it is used routinely.

**Managing patients after discharge**

Many patients with delirium are discharged before their symptoms are fully resolved; this factor must be accounted for in planning their care after discharge. The continuing need for rehabilitation must be explicitly documented. Problems with attention and orientation are especially persistent.\(^8\) Further episodes may be prevented by addressing risk factors such as medication and sensory impairment. The psychological sequelae of delirium have not been studied enough, but depression and post traumatic stress disorder have been described. Most patients dismiss the episode of delirium once it has passed, but a significant minority have lingering concerns that an episode of delirium may represent the first step towards loss of mental faculties and independence.\(^9\) Other patients experience “silent delirium” and are ashamed or afraid to admit to symptoms. A post-hospital visit to the treatment environment can facilitate adjustment and clarify the transient nature of delirium symptoms.\(^10\)

**Conclusions**

There has been a shift towards recognising delirium as a distinct entity requiring study in its own right. This has resulted in greater appreciation of the variety of the syndrome’s symptoms and the development of accurate screening tools that can be readily applied in routine clinical practice. Optimal management of delirium primarily depends on reducing modifiable risk factors and detecting high risk cases early. Treatment requires multifaceted, interdisciplinary efforts that address both the underlying causes and the symptoms of delirium. The value of supportive and environmental strategies is increasingly being recognised, particularly in research designed and run by nurses. Typical neuroleptic drugs remain the cornerstone of treatment; however, their effectiveness in both acute and long term treatment in different populations in which delirium has different causes and for varying symptom profiles remains poorly studied. Benzodiazepines are the treatment of choice in delirium associated with specific causes, such as alcohol withdrawal, and are a useful adjunct treatment in other cases. Specific treatments for delirium, such as physostigmine and flumazenil, can be useful where rapid reduction in symptoms is desirable. Atypical neuroleptics and procholinergic agents have substantial treatment potential but have not been studied in depth. The symptoms of delirium frequently persist beyond the acute phase of treatment, therefore post-discharge treatment plans must focus on reducing ongoing risk factors and managing residual functional impairments.

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A painful hip as a presentation of Guillain-Barré syndrome in children

Tjun Tang, Charles Noble-Jamieson

Pain of the lower limb in children is a symptom of many conditions and can lead to diagnostic difficulties; the clinician may search for a musculoskeletal rather than a neurological cause. Guillain-Barré syndrome must be considered when a child presents with the lower limb. Misdiagnosis is more common in the paediatric population because the child's history and cooperation in the neurological examination are often limited. Failure to diagnose Guillain-Barré syndrome and to initiate prompt treatment is potentially life threatening as the disease can quickly lead to respiratory failure and death from muscle paralysis. We describe a child with Guillain-Barré syndrome who initially presented with a painful hip.

Case report

A two year old boy presented with pain in his right leg. Three weeks earlier he had had tonsillitis, fever, and diarrhoea. His doctor had treated him with amoxycillin, and his symptoms subsequently settled. The pain in his leg started two days before admission. He limped and was reluctant to walk. The pain was precipitated by walking and was vaguely localized to the hip. He had no other joint symptoms or relevant history. On examination he was apyreal but irritable. He had difficult sitting and refused to stand or weight bear. Neurological examination revealed intact cranial nerves, although the gag reflex was depressed, which was partly attributed to his uncooperative behaviour. However, there was no indication that he had been choking.

Examination of the upper limbs revealed normal tone and power, but reflexes of the biceps, triceps, and supinator were diminished. The patient was distressed on flexion, extension, and internal rotation of the right hip. Otherwise the joints had full range of movement, and C-reactive protein concentration gave normal results. An orthopaedic opinion was sought, and an irritable hip was considered likely. The patient was initially given paracetamol for analgesia, but his leg started two days before admission. He limped and was reluctant to walk. The pain was precipitated by walking and was vaguely localized to the hip. He had no other joint symptoms or relevant history. On examination he was apyreal but irritable. He had difficult sitting and refused to stand or weight bear. Neurological examination revealed intact cranial nerves, although the gag reflex was depressed, which was partly attributed to his uncooperative behaviour. However, there was no indication that he had been choking.

Lesson of the week

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Examination of the upper limbs revealed normal tone and power, but reflexes of the biceps, triceps, and supinator were diminished. The patient was distressed on flexion, extension, and internal rotation of the right hip. Otherwise the joints had full range of movement with no swelling or tenderness, although the patient preferred to lie with his hips flexed and mildly rotated externally. The patella and ankle reflexes were diminished bilaterally. The plantar responses were extensor.

Ultrasonography of the hips showed a symmetrical appearance with no synovial thickening or effusions. A radiograph of the hips showed a slightly irregular epiphysis on the right side but otherwise gave normal results. A bone scan was later performed, but no definitive abnormality was found.

Tests for blood count, erythrocyte sedimentation rate, and C-reactive protein concentration gave normal results. An orthopaedic opinion was sought, and an irritable hip was considered likely. The patient was initially given paracetamol for analgesia, but because of increasing hip pain and irritability he was given Oramorph (Boehringer Ingelheim) and his right leg was placed on skin traction.

On day 4 after admission he continued to deteriorate; he mentioned pain in his neck, elbows, and wrist. He became weak, lethargic, and disinterested in feeds. He was unable to sit up independently. A musculoskeletal cause was considered, and he was referred to a rheumatologist at a tertiary centre. On examination only generalised limb weakness and hypotonia were found, and a neurological opinion was subsequently sought. By this time he had started to cough and was...