BMJ Best Practice

Assessment of altered mental status

Straight to the point of care

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Table of Contents

Summary

Altered mental status (AMS) is a general term used to describe various disorders of mental functioning ranging from slight confusion to coma.[1] Given the vagueness of the term, it is imperative to understand its key components before considering a differential diagnosis. Fundamentally, mental status is a combination of the patient's level of consciousness (i.e., attentiveness) and cognition (i.e., mental processes or thoughts); patients may have disorders of one or both.[2] For example, patients with meningitis may have impaired consciousness (i.e., altered sensorium, decreased attentiveness) with intact cognition, whereas patients with dementia may have a normal level of consciousness with impaired cognition. However, more frequently, patients exhibit altered levels of consciousness plus cognition: for example, with delirium, a relatively common and sometimes fatal cause of AMS.

Epidemiology

An observational study conducted in the accident and emergency department found that acutely altered mental status was the primary reason for the visit for about 1% of all adult patients and 2.4% of older adults.[3] About 40% of patients were aged over 60 years. Thirty-five percent of cases had a neurological cause (e.g., stroke, traumatic brain injury, or seizures). Acute alcohol intoxication, infection, and metabolic abnormalities were other common causes of AMS.[3]

Another observational study reported that over half of adults aged over 65 years with AMS had delirium. Mortality was almost 25%, and the mortality rate increased if AMS lasted longer than 3 days. In this group, infection and neurological disease were the most common aetiologies.[4]

Levels of consciousness

Normal state of consciousness consists of either the state of attentiveness in which most people function while not asleep, or one of the recognised stages of normal sleep from which the person can be easily aroused. Abnormal state of consciousness is more difficult to categorise, and many terms are used. Some of the more common terms include:[5] [6]

- Hyper-alert: heightened arousal with increased sensitivity to immediate surroundings. Hyper-alert patients can be verbally and physically threatening, restless, and/or aggressive.
- Confused: disorientated; bewildered, and having difficulty following commands.
- Delirious: disorientated; restless, hallucinating, sometimes delusional.
- Somnolent: sleepy, responding to stimuli only with incoherent mumbles or disorganised movements.
- Lethargic: reduced level of alertness with decreased interest in the surrounding environment.
- Obtunded: similar to lethargy; the patient has a lessened interest in the environment, has slowed responses to stimulation, and tends to sleep more than normal, with drowsiness in between sleep states.
- Stuporous: profoundly reduced alertness and requiring continuous noxious stimuli for arousal.
- Comatose: state of deep, unarousable, sustained unconsciousness.[6]

Aetiology

The most common causes of AMS are cerebrovascular, traumatic, neurological, cardiac, psychiatric, metabolic, pulmonary, endocrinological, infectious, gastrointestinal, or exogenous. They either directly affect the central nervous system (CNS) or have a secondary neurological impact.[1] An observational study of people aged 65 years and older presenting with AMS (≤1 week) to four accident and emergency departments in Turkey found that the most common aetiology was infection (39.5%), followed by neurological disease (36.5%).[4] Almost any stress can present as AMS in infants, older people, or debilitated patients.

Cerebrovascular

By directly affecting the CNS, the following cerebrovascular causes can alter mental status: stroke, subdural haematoma, epidural haematoma, and subarachnoid haemorrhage.

Traumatic

Head injuries (e.g., concussions, traumatic brain injuries) are common conditions that alter mental status.[7] Hip tenderness might suggest occult hip fracture, a frequently missed trigger for delirium in frail older patients, particularly if they are bed-bound.[8] [9] [10]

Neurological

Dementia, delirium, seizures (status epilepticus or postictal states), tumours, hypertensive encephalopathy, non-convulsive status epilepticus, and Wernicke's encephalopathy may all alter mental state.

Cardiac and pulmonary

Systemic diseases that have neurological consequences include cardiac disorders such as myocardial infarction, congestive heart failure, and arrhythmias. Pulmonary embolism, hypoxia, and carbon monoxide poisoning are other diagnoses that may result in AMS.

Psychiatric

Acute psychoses can alter neurological function. Patients with acute psychosis typically show 1 or more of the following signs or symptoms: delusions, hallucinations, disorganised speech, or grossly disorganised or catatonic behaviour lasting >24 hours but <30 days. Depression (including catatonia) and bipolar mania may also present as AMS.

Metabolic

The following metabolic conditions/imbalances can have neurological consequences: dehydration; hepatic encephalopathy; uraemia; hypothermia and hyperthermia; hypercapnia; hypo/hypernatraemia; hypo/hyperglycaemia; and hyper/hypocalcaemia. Mental status changes in patients with ketoacidosis should alert clinicians to other potential causes, such as toxic ingestion, hypoglycaemia, alcohol-withdrawal seizures, postictal state, or unrecognised head injury.

Endocrinological

Adrenal insufficiency, thyrotoxicosis, myxoedema coma, and pituitary infarction can result in AMS.

Infectious

Meningitis, acute systemic infections (e.g., pneumonia, urinary tract infection, skin/soft-tissue infections, cholecystitis), encephalitis, neurosyphilis, and brain abscesses can alter mental status.

Gastrointestinal

This group (notwithstanding surgical conditions in other anatomical locations) includes mesenteric ischaemia, diverticulitis, appendicitis, and constipation. The latter can be associated with hypercalcaemia or myxoedema coma.

Exogenous

Common exogenous toxins that can cause AMS include medications, such as anticholinergics, sympathomimetics, antihistamines, anti-emetics, opioids, antiparkinsonian medications, and antispasmodics.

Withdrawal from alcohol and sedatives can also precipitate changes in mental function.

Illicit drugs such as opiates, amfetamines, cocaine, and hallucinogens are frequently implicated.

Urgent considerations

(See **Differentials** for more details)
Rapid assessment and stabilisation of a patient with AMS is mandatory, to include the immediate assessment of airway, breathing, circulation, and vital signs. This includes checking for and treating reversible causes of the altered mental condition (e.g., giving oxygen, thiamine, glucose, naloxone), obtaining an accurate temperature measurement, ordering emergency head computed tomography (CT) if signs of trauma are present, giving empirical antibiotics (and/or antivirals) if fever is present, and taking other basic manoeuvres appropriate to the circumstances. Thiamine should be administered before glucose if Wernicke encephalopathy is suspected.

Acute neurological events

New-onset stroke or transient ischaemic attack, traumatic head injury, epidural or subdural haematoma, subarachnoid haemorrhage, seizures, meningitis, encephalitis, brain abscesses, and neurosyphilis can result in AMS.[11] Neurological assessment is prudent, with CT and/or magnetic resonance imaging (MRI).

Investigations in patients with signs of hypertensive encephalopathy should focus on any signs of end-organ damage. In cases of acute hypertensive emergency, the initial goal of therapy is to reduce mean arterial blood pressure (BP) by no more than 25% (within minutes to 1 hour), and then, if the patient is stable, to 160/100 to 110 mmHg within the next 2 to 6 hours.[12] [13]

Delirium (an acute, fluctuating level of consciousness and cognition characterised by inattentiveness and disorganised thinking) is a medical emergency that requires immediate work-up.[8] [14] History or signs indicating a general medical condition, such as infection, metabolic disturbance, or pharmacological toxicity, can sometimes be elucidated. Initial tests to order include full blood count (FBC), metabolic profile, fasting blood glucose, urinalysis, and urine culture. Further investigations and management are guided by clinical history and examination. Delirium in older patients admitted to hospital is frequently persistent (up to 21% of older patients at 6 months following discharge).[15] Patients with persistent delirium have consistently been shown to have worse clinical outcomes, including greater risk of losing their independence and being placed in long-term care.[15]

Severe systemic infection

Considering occult infections (central nervous system, skin, heart, lung, abdomen, genitourinary) is imperative, given that early recognition and treatment of sepsis or septic shock is key to improving outcomes.[16] [17] [18] AMS may be the only identifiable sign of urinary tract infections and pneumonia in older people. Urinalysis and chest x-ray should be obtained as part of every work-up. Brain abscesses can also present with AMS, and can be identified by CT or MRI scans of the head.

Sepsis

A spectrum of disease, where there is a systemic and dysregulated host response to an infection.[19] Presentation ranges from subtle, non-specific symptoms (e.g., feeling unwell with a normal temperature) to severe symptoms with evidence of multi-organ dysfunction and septic shock. Patients may have signs of tachycardia, tachypnoea, hypotension, fever or hypothermia, poor capillary refill, mottled or ashen skin, cyanosis, newly altered mental state, or reduced urine output.[17] Sepsis and septic shock are medical emergencies.

Risk factors for sepsis include:[17]

- age under 1 year
- age over 75 years
- frailty
- impaired immunity (due to illness or drugs)
- recent surgery or other invasive procedures
- any breach of skin integrity (e.g., cuts, burns)
- intravenous drug misuse
- indwelling lines or catheters
- pregnancy or recent pregnancy.

Early recognition of sepsis is essential because early treatment improves outcomes.[17] [18][Evidence C] [Evidence C] However, detection can be challenging because the clinical presentation of sepsis can be subtle and non-specific. A low threshold for suspecting sepsis is therefore important. The key to early recognition is the systematic identification of any patient who has signs or symptoms suggestive of infection and is at risk of deterioration due to organ dysfunction. Several risk stratification approaches have been proposed. All rely on a structured clinical assessment and recording of the patient's vital signs.[17] [20] [21][22] [23] It is important to check local guidance for information on which approach your institution recommends. The timeline of ensuing investigations and treatment should be guided by this early assessment.[22]

Treatment guidelines have been produced by the Surviving Sepsis Campaign and remain the most widely accepted standards.[18] [24] Recommended treatment of patients with suspected sepsis is:

- Measure lactate level, and re-measure lactate if initial lactate is elevated (>2 mmol/L [>18 mg/dL]).
- Obtain blood cultures before administering antibiotics.
- Administer broad-spectrum antibiotics (with methicillin-resistant *Staphylococcus aureus* [MRSA] coverage if there is high risk of MRSA) for adults with possible septic shock or a high likelihood for sepsis.
- For adults with sepsis or septic shock at high risk of fungal infection, empirical antifungal therapy should be administered.
- Begin rapid administration of crystalloid fluids for hypotension or lactate level ≥4 mmol/L (≥36 mg/dL). Consult local protocols.
- Administer vasopressors peripherally if the patient is hypotensive during or after fluid resuscitation to maintain MAP ≥65 mm Hg, rather than delaying initiation until central venous access is secured. Noradrenaline is the vasopressor of choice.
- For adults with sepsis-induced hypoxaemic respiratory failure, high-flow nasal oxygen should be given.

Ideally, these interventions should all begin in the first hour after sepsis recognition.[24]

For adults with possible sepsis without shock, if concern for infection persists, antibiotics should be given within 3 hours from the time when sepsis was first recognised.[18] For adults with a low likelihood of infection and without shock, antibiotics can be deferred while continuing to closely monitor the patient.[18]

For more information on sepsis, please see our topics [Related Topic: Sepsis in adults] and [Related Topic: Sepsis in children].

Gastrointestinal

Appendicitis and acute mesenteric ischaemia are surgical emergencies that can be fatal if not identified and treated.

Appendicitis causes constant mid-abdominal pain that later moves to the right lower quadrant. The pain is usually worse on movement. Anorexia, nausea, and vomiting are common. One classic sign is right lower quadrant abdominal tenderness (McBurney's sign). There may be localised rebound tenderness, especially if the appendix is anterior. The goal of treatment is to remove the infected appendix. Once the diagnosis of acute appendicitis is made, patients should be given nothing by mouth. Intravenous maintenance fluids should be started and appendectomy performed without delay.

The majority of patients with an ischaemic bowel experience pain, which can vary depending on the type and segment of bowel involved. Haematochezia, melaena, and diarrhoea frequently occur. Perceived pain may be out of proportion to tenderness appreciated on physical examination. Adequate fluid resuscitation and supplemental oxygen should be administered to optimise tissue perfusion and oxygenation. Initial resuscitation should also aim to relieve any acute heart failure and correct any cardiac arrhythmias. Invasive monitoring and inotropic support may be appropriate. Nothing-by-mouth status should be enforced, with nasogastric tube decompression for symptomatic relief.

Empirical antibiotics suitable for enteric coverage are administered to all patients according to local antimicrobial guidelines, as ischaemia can lead to significant bacterial translocation due to damage to the normal intestinal mucosal barrier.

With the emergence of interventional radiology, endovascular treatment may be considered for haemodynamically stable patients where available. If there are clinical signs of peritonitis, or radiographic or laboratory evidence suggestive of infarction or perforation, exploratory laparotomy or laparoscopy must proceed urgently and include resection of non-viable intestine.

Cardiac events

Acute chest pain warrants rapid clinical assessment, as underlying disease can be life-threatening. Continuous monitoring of pulse, BP, and oxygen saturation is standard care. If the patient is in pain or breathless, or oxygen saturation is <90%, high-flow oxygen should be given. Morphine (intravenous) may also be necessary to relieve severe pain.

Initial investigations include a 12-lead ECG, chest x-ray, cardiac biomarkers, FBC, and renal profile. The patient may need to be transferred to an intensive care setting. Once the patient is stable, further tests, such as a ventilation-perfusion scan, echocardiogram, CT, or angiography, should be requested to confirm clinical suspicion.

Psychiatric events

The assessment of an acutely psychotic patient includes a thorough history and physical examination, as well as laboratory tests. Based on the initial findings, further diagnostic tests may be warranted. Organic causes must be considered and excluded before the psychosis is attributed to a primary psychotic disorder. The most common cause of acute psychosis is drug toxicity from recreational, prescription, or non-prescription drugs. Patients with structural brain conditions, or a toxic or metabolic process presenting with psychosis, usually have other physical manifestations that are readily detectable by history, neurological examination, or routine laboratory tests.

Respiratory disorders

AMS is commonly associated with hypoxia that is usually secondary to an underlying disease, such as systemic infection, pulmonary embolism, severe asthma attack, COPD, cardiac failure or arrhythmia, or carbon monoxide poisoning. Pulse oximetry and arterial blood gases can confirm the presence of hypoxia.

Medication effects

It is essential to establish whether new medications have been started, an existing medication has been recently changed, or a medication has been stopped abruptly.[25] Enquiries should include questions about non-prescription medications and surreptitious alcohol use. Medication reconciliation is mandatory in the emergency department, as certain withdrawal states can be fatal if missed.

Toxidromes

A toxicology screen (for both prescription and illicit drugs) and an alcohol level should be ordered whenever substance abuse is suspected. Accidental poisoning should be considered in all young children with acute mental status changes, and management should be dictated based on the suspected toxin. Withdrawal syndromes should also be considered. Rapid diagnosis and urgent treatment of all toxidromes is imperative. Consideration must be given to illicit drug use (e.g., opiate, amfetamine, and benzodiazepine abuse).

Endocrinopathies

Myxoedema coma typically occurs in older patients with underlying hypothyroidism. Adrenal crisis can occur in patients with Addison's disease during stress, trauma, or infection or, more commonly, in those taking corticosteroids. Thyroid function tests and serum cortisol levels should be considered as part of the work-up for AMS.

Adrenal crisis should be treated immediately, even if a laboratory diagnosis has not yet been made. Intravenous hydrocortisone is given if adrenal crisis is clinically suspected.

Intravenous fluids should be administered to correct hypotension and dehydration. This may be the most important component in the immediate resuscitation of a critically ill patient. Careful monitoring of BP, fluid status, and serum sodium and potassium levels should be maintained. Glucose should be administered when necessary to correct hypoglycaemia, but care should be taken to avoid worsening hyponatraemia. The use of normal saline supplemented with dextrose 5% is helpful in this regard.

Metabolic abnormalities

Patients with life-threatening cases of sodium, potassium, and calcium abnormalities may present with AMS. Metabolic abnormalities may be secondary to renal or liver disease. A metabolic work-up is essential.

Glucose abnormalities

Both hypoglycaemia and hyperglycaemia can present with confusion and reduced consciousness. Plasma glucose should be the first test in any patient presenting with AMS, as it is quick and easy to measure and readily treatable. If the test is not immediately available, empirical glucose should be given.

Approach

Although AMS is common in presentation, its work-up is challenging because there are many potential causes, ranging from less serious to life-threatening. Therefore, a thoughtful, comprehensive approach is essential, which involves clarifying the history and onset of symptoms with the patient and/or carers, and localising specific signs or symptoms to narrow the differential.

Assessing a patient with AMS is difficult because obtaining a reliable history from the patient is often impossible. Initially, it is imperative to establish basic life support.[6] Once the patient's airway, breathing, and circulation have been secured, a secondary emergency survey should be conducted. See Urgent considerations section for conditions requiring immediate management.

After emergency treatment and stabilisation of the patient, a directed differential diagnosis should be considered. Older patients often present with relatively common conditions in uncommon, subtle manners. For example, they may present with infections without fever or leukocytosis, or a perforated viscus without abdominal pain or tenderness. It is therefore important to adopt a logical, stepwise approach.

Healthcare professionals often fail to recognise and diagnose delirium in older patients.[26] [27] There are multiple validated assessment tools for delirium.

- The Confusion Assessment Method (CAM), the CAM Short Form (CAM-S), and the brief CAM (bCAM) can be used to diagnose delirium, focusing on four cardinal features:[28] [29] [30] [31]
    - Acute onset and fluctuating course
    - Inattention
    - Disorganised thinking
    - Altered level of consciousness.

  CAM is a well-validated tool for assessing delirium, with a reported sensitivity of 87% to 100% and specificity of 80% to 100%.[32] CAM is specific for assessing incident delirium in critically ill older patients (although its sensitivity may be lower than that of some other screening tools), and it is commonly used to determine delirium severity (as are the Delirium Rating Scale [DRS] and the Memorial Delirium Assessment Scale).[33] [34]
- The Observational Scale of Level of Arousal (OSLA) is a bedside assessment tool, which has a sensitivity of over 90% and a specificity of over 80% for diagnosing delirium in older patients.[35] The assessment is based on patient observations in four clinical areas: eye contact, eye opening, posture, and movement. UK guidelines recommend that clinicians consider using OSLA to distinguish between dementia and delirium in people who have not been diagnosed with either condition.[36]
- 4AT is a brief tool that combines four elements:[8] [37]
    - Alertness: anything less than A on the alert, voice, pain, unresponsive (AVPU) scale
    - AMT4: four questions from the Abbreviated Mental Test (age, date of birth, place, and current year)
    - Cognition: recite the months backwards (December to July only)
    - Acute change or fluctuating course.

History

Initially determine a baseline level of mental status/cognition, and establish the rapidity with which changes have occurred. This often requires the assistance of a third party, such as a relative, spouse, or friend.

Questions should be targeted at establishing recent events, such as trauma, relevant past medical history, previous medication use, and use of alcohol or toxins. Every body system should be assessed in an attempt to localise the potential aetiology.

Key historical considerations include the following:

- Previous cognitive status: it is imperative to establish a baseline cognitive and functional status before the onset of symptoms. In most cases, a rough assessment of previous cognitive status can be obtained from the patient's family. A previously obtained assessment of cognition can also be compared with a current screen to determine whether symptoms related to cognitive changes are acute or chronic in nature. The Folstein Mini-Mental State Examination (MMSE) is still the most widely used cognitive screening test.[38] However, it has been increasingly shown in the literature to be poorly sensitive in differentiating mild cognitive impairment from a dementia syndrome, due largely to the MMSE's lack of executive function testing.[39] [40] [41] There are several other tests available, including the 10-minute Montreal Cognitive Assessment Scale (MoCA).[42] [43] [44] Some instruments, such as the Mini-Cog test and Addenbrooke's Cognitive Examination-Revised (ACE-R), have been shown to perform as well as the MMSE in terms of detecting dementia.[41] Existing tools for evaluating delirium superimposed on dementia lack robust evidence to support their utility; however, results obtained with the CAM and CAM-ICU are promising.[45] [46]
- It is noteworthy that fluent aphasia (e.g., Wernicke's encephalopathy) can sometimes be mistaken for delirium or AMS, particularly when other neurological signs are not present. Therefore, short tests for aphasia (e.g., object naming, phrase repetition, following simple commands) should be conducted in differentiating this condition.
- Previous functional status: care should be taken to determine whether the patient has deficiencies in activities of daily living, hearing impairment, or vision impairment.
- Medication usage: medication lists should be carefully scrutinised. Potentially high-risk medications should be discontinued whenever possible. Herbal remedies, non-prescription medications, and illicit substances should also be considered in a medication review.
- Comorbid conditions: particularly neurological diseases (e.g., stroke, Parkinson's disease, dementia), cardiovascular diseases (e.g., myocardial infarction [MI], angina), and a history of renal/metabolic diseases (e.g., hyponatraemia, hypernatraemia, chronic renal failure).
- Pain levels: the presence of severe pain is often associated with AMS. Chest pain (often described as heavy, or tight) radiating to arms, back, neck, or jaw is typical with MI, although chest pain may be absent in older adults and people with diabetes.
- Alcohol and drug use: alcohol intoxication and withdrawal are frequently associated with altered mental status.
- Non-specific irritability: together with typical symptoms of sweating, palpitations, weight loss, may suggest thyrotoxicosis.
- Environmental factors: key issues, such as sleep deprivation, multiple procedures or surgery, restraint use, and intensive care stay, are associated with delirium and might be causative. Hypothermia may be suspected if there is a recent history of exposure to the cold for a prolonged period of time, or with inadequately warm clothing. This is more common in older adults, or in young children and infants. Alternatively, heat stroke may be suspected following intense exercise under hot, humid conditions.

Physical examination

Possible helpful findings include signs of head trauma, icterus, hydration status, dry mouth, a bitten tongue, nuchal rigidity, heart murmurs, and abdominal tenderness. Important considerations include the following.

- Pupillary response: might suggest drug intoxication, drug withdrawal, or stroke.
- Vital signs: may be particularly revealing, either in a toxidrome pattern, such as anticholinergic toxicity (e.g., fever, tachycardia, hypertension), or in a pattern of autonomic dysfunction, as in alcohol withdrawal, although this may be blunted in older people. Bradycardia and hypotension reflect possible myxoedema coma or heart block. Bradycardia and hypertension can be signs of elevated intracranial pressure. Tachycardia and hypotension may suggest shock from either cardiogenic or hypovolaemic aetiologies.
- Fever: may be helpful for distinguishing infection. Hyperthermia (e.g., with heat stroke) is generally associated with core temperatures >40°C (>104°F). Sweating, together with palpitations, weight loss, and irritability, may suggest thyrotoxicosis.
- Core body temperature: lowered to <35°C (<95°F) if hypothermic. Low-reading infrared tympanic membrane thermometers should be used.
- Neck stiffness: meningitis or encephalitis should be considered.
- Lung examination: decreased breath sounds and rales might indicate infection (e.g., pneumonia) or diseases commonly associated with hypoxia such as congestive heart failure (CHF) and COPD.
- Cardiovascular examination: physical findings evident with coronary disease or MI should be assessed.
- Abdominal examination: might suggest intra-abdominal infection. If the history and physical examination findings suggest constipation, secondary causes need to be ruled out. Features of intestinal obstruction may be present.
- Suprapubic tenderness or palpable bladder: might suggest urinary tract infection (UTI) or obstruction.
- Hip tenderness: might suggest occult hip fracture, a frequently missed trigger for delirium in frail older patients, particularly if they are bed-bound.
- Neurological findings: focal findings might suggest stroke or neurological insult. The investigation should include cranial nerve testing (including visual fields); motor examination (to assess focality and possible parkinsonism); sensory (often difficult in a patient with AMS), cerebellar, and verbal abilities; and gait.

Investigations

Investigations should be guided by history and physical examination findings.[25] In the absence of definitive historical or physical findings, a preliminary work-up should include the following:

- Plasma glucose should be the first test in any patient presenting with AMS; it is quick and easy to perform, and abnormalities are readily treatable. If the test is not immediately available, empirical glucose should be given.
- FBC to confirm suspected anaemia and help in the diagnosis of infection.
- Chemistry profile, including glucose levels, to rule out metabolic disturbances.
- Thyroid function tests if thyrotoxicosis or myxoedema coma is suspected.
- Urinalysis to rule out UTI.
- Chest x-ray to help detect pneumonia, CHF, or other potential causes of hypoxia.
- Drug levels in patients on digoxin, lithium, quinidine, and alcohol (if a history of alcohol abuse is suspected).

- ECG and cardiac enzymes to rule out MI.[6]
- Arterial blood gas or pulse oximetry to evaluate for hypoxia and lactate, commonly found in sepsis, or hypercapnia.
- If liver dysfunction is suspected, liver function tests, including bilirubin, are warranted; coagulation studies may be abnormal. Plasma ammonia measurement should be performed in patients with delirium/encephalopathy and liver disease.[47]
- If infection is suspected, blood and urine culture should be obtained. Lumbar puncture is recommended in the presence of nuchal rigidity and fever, or if encephalitis is suspected.
- If a hip fracture is suspected as a cause of AMS (e.g., with a history of a fall and age above 65 years), a pelvic x-ray and consideration of a hip computed tomography (CT) scan (e.g., in patients with persistent pain, concerning examination findings, no obvious fracture visible on x-ray) or bone scan may be helpful.

If no aetiology is identified from preliminary testing, further investigations should be considered including the following:

- Neurological imaging (CT and/or magnetic resonance imaging).
- Holter monitor, exercise testing, and/or cardiac electrophysiology studies to assess for arrhythmias.
- Coronary angiography to rule out ischaemic heart disease.
- Echocardiography to assess for cardiac failure and cardiomyopathy.
- B-type natriuretic peptide to assess for cardiac failure.
- CT pulmonary angiogram or ventilation-perfusion scan to assess for pulmonary embolism as a cause of hypoxia.
- Glomerular filtration rate may be useful in uraemia.
- Abdominal imaging and/or endoscopy if abdominal pathology such as acute appendicitis or bowel ischaemia is suspected.
- EEG to rule out seizure activity and encephalopathy. Diffuse slowing of the EEG may be helpful in highlighting delirium.[48]
- A therapeutic trial of parenteral thiamine if Wernicke's encephalopathy is suspected.

Urgent brain imaging is needed in the presence of rapid deterioration of mental status, and may be done simultaneously with or even before some laboratory tests under certain circumstances (e.g., suspected stroke or intracranial haemorrhage). If the diagnosis of dementia is being considered, a CT scan of the head is useful for excluding tumours, normal pressure hydrocephalus, and subdural haematoma. Investigations in patients with signs of hypertensive encephalopathy should focus on any signs of end-organ damage. In addition, spot urine or plasma metanephrine may be useful before initiation of drug therapy to rule out phaeochromocytoma in these patients.

Differentials overview

Common
Stroke and transient ischaemic attack
Head injury
Dementia
Delirium
Seizures with possible postictal state
Myocardial infarction
Congestive heart failure
Ventricular arrhythmias
Depression
Hyperglycaemia
Hypoglycaemia
Hypernatraemia
Hyponatraemia
Dehydration (volume depletion)
Hypothermia
Hypoxia
Hypercapnia
Hepatic encephalopathy
Uraemia
Severe systemic infection
Bipolar disorder

Common

- Brief psychotic disorder
- Alcohol withdrawal
- Alcohol toxicity
- Drug toxicity
- Drug withdrawal
- Hip fracture
- Pulmonary embolism

Uncommon

- Subdural haematoma
- Epidural haematoma
- Subarachnoid haemorrhage
- Brain tumour
- Non-convulsive status epilepticus
- Hypertensive encephalopathy
- Wernicke's encephalopathy (thiamine deficiency)
- Hypercalcaemia
- Hypocalcaemia
- Carbon monoxide poisoning
- Hyperthermia
- Adrenal insufficiency
- Thyrotoxicosis
- Myxoedema coma

Uncommon
Pituitary apoplexy
Meningitis
Encephalitis
Neurosyphilis
Brain abscess
Mesenteric ischaemia
Appendicitis
Acute diverticulitis
Constipation

Differentials

Common

Stroke and transient ischaemic attack

History	Exam	1st Test	Other tests
acute changes in mental status likely; associated with neurological symptoms: unilateral weakness or numbness; change in vision (unilateral or bilateral); difficulty with speech, comprehension; loss of coordination, difficulty walking; severe headache, anosognosia, neglect syndromes[49]	confusion frequently noted; focal neurological signs include: unilateral hemiparesis, hemianopia, aphasia, ataxia[49]	»**CT and/or MRI head:** ischaemic stroke: hyperdense vessels at site of blood clot in middle cerebral artery (MCA), posterior cerebral artery, or anterior cerebral artery; loss of insular stripe located between sylvian fissure and basal ganglia is frequently associated with early MCA stroke; subtle mass effect; haemorrhagic stroke: hyperdense to grey matter lesion at site of haemorrhage; mass effect may also be evident but frequently subtle in early stroke findings, frequently absent for transient ischaemic attacks and ischaemic strokes	

Head injury

History	Exam	1st Test	Other tests
history of trauma, often accompanied by change in level of consciousness or headache and dizziness	external evidence of trauma: bruising, bleeding, raccoon eyes, fractures, watery nasal discharge (cerebrospinal fluid rhinorrhoea)	»**CT head:** intracranial haemorrhage (epidural, subdural, and/or intracerebral), skull fracture and/or contusion	

◊ Dementia

History	Exam	1st Test	Other tests
insidious, chronic decline in both memory	disorientation to person, place, or time	»**none:** diagnosis is clinical	»**CT scan head:** excludes space-

Common

◊ Dementia

History	Exam	1st Test	Other tests
and at least one other cognitive domain (executive function, language, visual-spatial) that interferes with daily life	and possibly otherwise normal; suggestive score on mini-mental examination	Patient's current level of cognitive/ functional capabilities is compared with premorbid level. Diagnosis considered by means of history, cognitive examination, physical examination, laboratory tests, and neuroimaging. Developments in biomarkers continue to increase diagnostic certainty.[14] [50] [51]	occupying lesions or other pathology Useful for excluding tumours, normal pressure hydrocephalus, and subdural haematoma.

Delirium

History	Exam	1st Test	Other tests
acute, fluctuating change in mental status; underlying cognitive impairment; advanced age, recent surgical intervention, underlying infection; may accompany hip fracture	characterised by inattention, disorganised thinking, and altered levels of consciousness on neurological examination; may have hip or pelvic tenderness with manipulation of joint	»**none:** diagnosis is clinical	»**CT scan head:** may exclude space-occupying lesions or other pathology Useful in excluding tumours, normal pressure hydrocephalus, subdural haematoma, or vascular disease.

Seizures with possible postictal state

History	Exam	1st Test	Other tests
loss of consciousness, observed seizure activity, urinary incontinence, tongue trauma; may report premonitory symptoms or signs	observed tonic-clonic seizure or abnormal movements followed by drowsiness	»**electroencephalogram:** synchronous epileptiform activity during a seizure; slowing of background elements, dampened reactivity, and loss of normal architecture	»**MRI or CT head:** usually normal, may show focal abnormalities

Common

Seizures with possible postictal state

History	Exam	1st Test	Other tests
		immediately after a seizure	

Myocardial infarction

History	Exam	1st Test	Other tests
history of risk factors for coronary artery disease (CAD) (e.g., of smoking, hyperlipidaemia, diabetes, family history of CAD); chest pain (often described as heavy, or tight) radiating to arms, back, neck, or jaw; chest pain may be absent in older adults and people with diabetes; dyspnoea; nausea; diaphoresis	hypotension; diaphoretic appearance; pallor; tachycardia; bradycardia; new abnormal pulse rhythm; distended jugular veins; other signs of heart failure (e.g, dyspnoea, crackles at lung bases); new heart murmur; delirium is often the only identifiable sign in older patients	»**ECG:** ST-segment elevation or depression, or T-wave changes »**cardiac enzymes:** elevated »**chest x-ray:** may show evidence of pulmonary congestion/ pleural effusion if secondary heart failure, may show enlarged cardiac shadow »**coronary angiogram:** presence of thrombus with occlusion of the coronary artery	

Congestive heart failure

History	Exam	1st Test	Other tests
shortness of breath, ankle swelling, orthopnoea, paroxysmal nocturnal dyspnoea, history of cardiac risk factors, previous myocardial infarction, valvular heart disease	jugular venous distension, orthopnoea, lower-extremity swelling, crackles in chest on auscultation, increased respiratory rate, third heart sound gallop rhythm on cardiac auscultation	»**echocardiography:** depressed ejection fraction, decreased systolic left ventricular function Sometimes can be normal in the presence of diastolic dysfunction.	»**b-type natriuretic peptide:** >100 nanograms/L (100 picograms/mL) indicates heart failure »**chest x-ray:** pulmonary oedema; Kerley A, B, and C lines; cardiomegaly Sometimes difficult to differentiate from acute respiratory distress syndrome.

Common

Ventricular arrhythmias

History	Exam	1st Test	Other tests
recent myocardial infarction (MI); history of coronary artery disease, previous cardiac arrest, mitral or aortic valve stenosis, or structural heart disease; family history of sudden death; may occur in supine position or with exertion; absent or brief prodrome (<5 seconds) of palpitation and light-headedness preceding syncope; valve replacement within the last 6 months	may be asymptomatic at presentation with no physical finding; or have hypoxaemia, pulmonary rales, jugular venous distension, and hypotension	»**ECG:** prolonged QT interval; delta waves if Wolff-Parkinson-White syndrome »**cardiac enzymes:** normal, unless associated with MI	»**chest x-ray:** increased alveolar markings, cardiomegaly Pulmonary oedema causes increased alveolar markings and can be caused by ischaemia secondary to ventricular arrhythmias. Cardiomegaly suggests concomitant congestive heart failure. »**echocardiography:** hypertrophic cardiomyopathy, valvular heart disease, low ejection fraction »**Holter monitor:** multiform premature ventricular complexes, couplets, non-sustained ventricular tachycardia (VT) event monitor: arrhythmias associated with symptoms »**exercise test:** exercise-induced arrhythmia »**electrophysiological studies:** induction of monomorphic VT; congenital long QT syndrome; catecholaminergic polymorphic VT »**coronary angiography:** coronary obstruction, congenital abnormalities, valvular abnormalities, coronary anomalies

Common

Ventricular arrhythmias

History	Exam	1st Test	Other tests
			Cardiac abnormalities can predispose to arrhythmias.

◊ Depression

History	Exam	1st Test	Other tests
persistent low mood, anhedonia, fatigue, disturbed sleep, poor concentration, altered appetite, feelings of guilt, agitation, or slowing of movements, suicidal thoughts; older age, recent childbirth, stress or trauma, female sex	weight change, diminished libido, melancholy, sleep disturbance, poor concentration	»**none:** diagnosis is clinical	

Hyperglycaemia

History	Exam	1st Test	Other tests
polyuria, polydipsia, weakness, nausea, vomiting, drowsiness, and weight loss, developing rapidly over a day or less; may be precipitated by infection, myocardial infarction, stroke, or other endocrine disorders (e.g., history of diabetes mellitus)	signs of volume depletion, including tachycardia and hypotension, Kussmaul's respiration, acetone breath, stupor, or coma	»**plasma glucose:** >13.9 mmol/L (>250 mg/dL) Should be measured as an initial laboratory assessment in diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state. »**serum electrolytes:** low sodium, chloride, magnesium, and calcium; elevated potassium »**urinalysis:** positive for glucose and ketones	»**ABG:** pH 7.0 to 7.3 Acidosis is a feature of DKA. Arterial pH measurement is necessary for diagnosis of DKA, but venous pH is recommended for monitoring treatment.

Common

Hypoglycaemia

History	Exam	1st Test	Other tests
sweating, nausea, headache, drowsiness, seizures; usually history of taking medication for diabetes, or alcohol abuse	tremor, sweating, tachycardia, focal neurological deficits, coma	»**plasma glucose:** <2.8 mmol/L (<50 mg/dL)	

Hypernatraemia

History	Exam	1st Test	Other tests
history of extrarenal fluid loss (e.g., vomiting, diarrhoea, burns); history of polyuria and polydipsia; diminished thirst response; inability to obtain fluid (e.g., bed-bound)	mental status changes, weakness, neuromuscular irritability, and/or coma/seizures[52]	»**serum electrolytes:** sodium >145 mmol/L (145 mEq/L)	

Hyponatraemia

History	Exam	1st Test	Other tests
anorexia, muscle cramps, headaches, altered mental status, including confusion, obtundation, coma, or status epilepticus; recent infection, recent medication change, and/or free water intoxication	confusion, seizures, coma[53]	»**serum electrolytes:** sodium <135 mmol/L (135 mEq/L)	

Dehydration (volume depletion)

History	Exam	1st Test	Other tests
thirst; fatigue; muscle cramps; abdominal pain; chest pain; confusion	dry mucous membranes; orthostatic hypotension; postural tachycardia; shock	»**FBC:** increased haematocrit; high haemoglobin »**serum electrolytes:** hyper- or	

Common

Dehydration (volume depletion)

History	Exam	1st Test	Other tests
		hypokalaemia; hyponatraemia »**urinalysis:** specific gravity >1.010 »**serum creatinine, urea:** urea/creatinine ratio >20	

Hypothermia

History	Exam	1st Test	Other tests
may be a history of being inappropriately dressed for a cold climate, or of being outside for a considerable amount of time; more common in older adults, children, and infants; may have increased urinary frequency	core body temperature lowered to <35°C (<95°F), measured using low-reading infrared tympanic membrane thermometer; early: increased respiratory rate, tachycardia, shivering, mood change, irritability, may show signs of frostbite; late: signs of pulmonary oedema, coma, bradycardia, ventricular arrhythmias	»**none:** diagnosis is clinical	»**ECG:** J wave or Osborn wave may be present

Hypoxia

History	Exam	1st Test	Other tests
usually secondary to underlying disease such as sepsis, pneumonia, pulmonary embolism, severe asthma attack, COPD, cardiac failure or arrhythmia, or carbon monoxide poisoning; symptoms include lack of coordination, poor judgement, seizures, myoclonic jerks, euphoria, nausea,	increased respiratory rate, tachycardia, cyanosis, poor coordination	»**pulse oximetry:** <95% oxygen saturation at sea level »**ABG:** diminished PO2 »**ECG:** tachycardia, arrhythmia, or ischaemia/infarction »**chest x-ray:** consolidation due to pneumonia, signs of infarction from pulmonary embolus, hyperinflation from	»**D-dimer:** positive if thromboembolic disorder »**multidetector CT scan of chest:** detection of thrombus in pulmonary artery Used in patients with a high suspicion of pulmonary embolus, or with positive D-dimer test.

Common

Hypoxia

History	Exam	1st Test	Other tests
visual impairment, coma		COPD, cardiomegaly from congestive heart failure	

Hypercapnia

History	Exam	1st Test	Other tests
dyspnoea; disturbed sleep; chest pain; confused; somnolent; obtunded	diffuse wheezing, hyperinflation (i.e., barrel chest), decreased breath sounds, hyperresonance on percussion; prolonged expiration; rhonchi, respiratory distress	»**ABG:** pH 7.0 to 7.3; PaCO2 >6 kPa (45 mmHg)	

Hepatic encephalopathy

History	Exam	1st Test	Other tests
historical findings might include history of hepatitis infection, alcohol use, and/or drug use; can be precipitated by infection, gastrointestinal bleeding, constipation, diuretic overdose	asterixis; jaundice, hepatomegaly, ascites may be present	»**clinical diagnosis:** hepatic encephalopathy is a clinical diagnosis; investigations are ordered to exclude other causes of brain dysfunction[55]	»**liver tests:** decreased or normal albumin; elevated or normal bilirubin; elevated or normal liver enzymes It is possible to have encephalopathy without abnormal liver function tests. In patients with delirium/ encephalopathy and liver disease, plasma ammonia should be measured, as a normal value brings the diagnosis of hepatic encephalopathy into question.[47]

Common

Hepatic encephalopathy

History	Exam	1st Test	Other tests
			»**coagulation tests:** elevated or normal prothrombin time »**CT head:** excludes intracranial haemorrhage or space occupying lesion

Uraemia

History	Exam	1st Test	Other tests
historical findings might include change in quantity or quality of urine output, anorexia, and/or non-steroidal anti-inflammatory drug use	myoclonic jerks; pallor, oedema, pleural effusion, pericarditis, neuropathy, and hypertension may be found	»**serum electrolytes, creatinine, urea:** creatinine >884 micromol/L (>10.0 mg/dL); elevated urea The degree to which creatinine predicts uraemic symptoms and renal failure is affected by multiple factors, including age, race, sex, and weight. »**glomerular filtration rate:** <10 mL/minute	

Severe systemic infection

History	Exam	1st Test	Other tests
symptoms of localised infection, non-specific symptoms include fever or shivering, dizziness, nausea and vomiting, muscle pain, feeling confused or disoriented; may be history of risk factors e.g., immunosuppression, pregnancy or postnatal period, frailty, recent surgery or	tachycardia, tachypnoea, hypotension, fever (>38°C) or hypothermia (<36°C), prolonged capillary refill, mottled or ashen skin, cyanosis, low oxygen saturation, newly altered mental state, reduced urine output	»**blood cultures:** may be positive for organism Blood cultures should be taken immediately, and preferably before antibiotics are started, provided their sampling will not delay administration of antibiotics. Other cultures (e.g., sputum,	»**ECG:** may show evidence of ischaemia, atrial fibrillation, or other arrhythmia; may be normal An ECG should be arranged to help exclude other differential diagnoses, including myocardial infarction, pericarditis, and myocarditis. Sepsis

Common

Severe systemic infection

History	Exam	1st Test	Other tests
invasive procedures, intravenous drug use or breach of skin integrity		stool, and urine) should be taken as clinically indicated. »**serum lactate:** may be elevated; levels >2 mmol/L (>18 mg/dL) associated with adverse prognosis; even worse prognosis with levels ≥4 mmol/L (≥36 mg/dL) Elevated serum lactate indicates tissue hypoperfusion, and is most reliably assessed using an arterial sample. »**FBC with differential:** WBC count >12×10⁹/L (12,000/microlitre) (leukocytosis); WBC count <4×10⁹/L (4000/microlitre) (leukopenia); or a normal WBC count with >10% immature forms; low platelets WBC count is sensitive but not specific for the diagnosis of sepsis. »**C-reactive protein:** elevated »**blood urea and serum electrolytes:** serum electrolytes may be deranged; blood urea may be elevated »**serum creatinine:** may be elevated Elevated creatinine may occur in sepsis associated with renal dysfunction.	also predisposes to myocardial dysfunction and arrhythmias. »**chest x-ray:** may show consolidation; demonstrates position of central venous catheter and tracheal tube »**urine microscopy and culture:** may be positive for nitrites, protein or blood; elevated leukocyte count; positive culture for organism »**sputum culture:** may be positive for organism »**lumbar puncture:** may be elevated WBC count, presence of organism on microscopy and positive culture Performed if meningitis suspected.

Common

Severe systemic infection

History	Exam	1st Test	Other tests
		»**liver function tests:** may show elevated bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and gamma glutamyl transpeptidase Sepsis can originate from hepatic or peri-hepatic infections. Comorbid hepatic disease can affect drug metabolism. Septic shock can compromise hepatic blood flow and metabolism. »**coagulation studies:** may be abnormal »**ABG:** may be hypoxia, hypercapnia, elevated anion gap, metabolic acidosis	

◊ Bipolar disorder

History	Exam	1st Test	Other tests
may have family history of psychiatric disorder; history of alternating episodes of mania, hypomania, and depression (although, despite being common, major depressive episode is not required for diagnosis of bipolar I disorder); requires fewer hours of sleep to feel rested, reports thoughts coming too	speech may be pressured with racing thoughts and flight of ideas during manic episodes; flat affect during depressive episodes; no findings suggestive of secondary cause of psychosis	»**psychiatric assessment:** diagnosis is clinical and made following exclusion of organic cause Use medical history, previous psychiatric diagnosis, and physician examination	»**FBC:** usually within normal range »**urine drug screen:** may be positive if concurrent drug use An acute psychotic episode is often triggered by drugs in patients with a background of a primary psychotic disorder. Care must

Common

◊ Bipolar disorder

History	Exam	1st Test	Other tests
fast to keep up with, distractible, increased goal-directed activities, excessive involvement in activities with high chance of painful consequences		to guide laboratory testing.[59]	be taken to distinguish primary psychotic disorders from drug-induced psychosis. »**serum thyroid-stimulating hormone:** usually within normal range »**serum free T4:** usually within normal range

Brief psychotic disorder

History	Exam	1st Test	Other tests
may have family history of psychiatric disorder; may be pregnant or have history of childbirth within last 4 weeks, or recent stress and trauma; history of ≥1 of delusions, hallucinations, disorganised speech, or disorganised or catatonic behaviour (at least one of these symptoms must be delusions, hallucinations, or disorganised speech), lasting at least 1 day but not >1 month, with eventual full return to premorbid level of functioning[14]	speech disorganised or pressurised, may jump from one subject to another with minimal connection, prolonged time elapsing between queries and answers (evidence of internal preoccupation), verbal responses to internal stimuli (evidence of hallucinations), delusions are generally very unstable and have rapidly changing topics, affect may be incongruent or flat, anxious, behaviour may be grossly disorganised or catatonic, changing moods are more common than in schizophrenia, may be bizarre, repetitive movements that appear goal directed but are carried out in a stiff fashion; no findings suggestive of secondary cause of psychosis	»**psychiatric assessment:** diagnosis is clinical and made following exclusion of organic cause Use medical history, previous psychiatric diagnosis, and physician examination to guide laboratory testing.[59] »**serum pregnancy test:** variable	»**urine drug screen:** may be positive if concurrent drug use An acute psychotic episode is often triggered by drugs in patients with a background of a primary psychotic disorder. Care must be taken to distinguish primary psychotic disorders from drug-induced psychosis. »**CT scan or MRI brain:** normal To rule out underlying neurological conditions as causes of the psychotic symptoms.

DIAGNOSIS

Common

Alcohol withdrawal

History	Exam	1st Test	Other tests
anorexia, sweating, anxiety, auditory or visual hallucinations, agitation, nausea, vomiting, headache, disorientation hours to days after abruptly decreasing alcohol intake	underweight, jaundice, enlarged or diminished liver size, ascites; diaphoresis; tachycardia; hypertension; fever; altered sensation (particularly in lower extremities); muscle tenderness on palpation; tremors, broad-based gait	»**blood alcohol level:** may be low if withdrawing »**LFTs including gamma glutamyl transferase:** elevated	

Alcohol toxicity

History	Exam	1st Test	Other tests
family history of alcoholism, antisocial behaviour, economic or legal concerns; anxiety, low responsivity to effects of alcohol, nausea, vomiting	jaundice, enlarged or diminished liver size, ascites; diaphoresis, haematemesis, tachycardia, hypertension, altered sensation (particularly in lower extremities); muscle tenderness to palpation, cramps	»**blood alcohol level:** elevated »**LFTs including gamma glutamyl transferase:** elevated	

Drug toxicity

History	Exam	1st Test	Other tests
overdoses with illicit or prescription drugs including anticholinergics, tricyclic antidepressants, stimulants, opiates, corticosteroids, analgesics, cardiac glycosides, and antiparkinsonian drugs can be associated with delirium; drug levels should be considered	anticholinergics: dry mouth, tachycardia, hypertension, absent bowel sounds; opiates: pinpoint pupils, decreased respirations	»**ECG:** arrhythmias associated with drug toxicity »**urine drug screen for illicit and prescription drugs:** measurable level of drug »**serum levels of drugs:** elevated	

Common

Drug withdrawal

History	Exam	1st Test	Other tests
abrupt cessation of drug (e.g., selective serotonin-reuptake inhibitors, benzodiazepine or barbiturate); nausea; confusion; hallucinations, including tactile hallucinations and delusions	agitation; malnourishment, poor hygiene, smell of alcohol, tremulous, tachycardia, hypertension, low-grade fever	»**urine drug screen:** normal »**blood alcohol level:** normal or low »**LFTs including gamma glutamyl transferase (gamma-GT):** gamma-GT elevated with recent alcohol	

Hip fracture

History	Exam	1st Test	Other tests
osteoporosis or osteopenia, age >65 years, female sex, low BMI and history of fall	pain in affected limb, groin, or proximal femur, with shortening and external rotation of the leg	»**pelvic x-ray:** fracture of proximal femur	»**CT pelvis:** presence of fracture line »**MRI of pelvis:** presence of marrow oedema and a fracture line »**technetium bone scan:** increased uptake of radioactivity in region of fracture

Pulmonary embolism

History	Exam	1st Test	Other tests
prolonged bed rest or immobility, pregnancy/postpartum period, inherited thrombophilias, active malignancy, recent trauma/fracture, and history of previous thrombosis; chest pain, feeling of apprehension, cough, haemoptysis, syncope	tachypnoea, dyspnoea, syncope, hypotension (systolic BP <90 mmHg), tachycardia, fever, elevated jugular venous pressure, sternal heave, accentuated pulmonary component of second heart sound, unilateral swelling/tenderness of calf	»**ECG:** atrial arrhythmias, right bundle branch block, inferior Q waves, precordial T-wave inversion, and ST segment changes suggest poor prognosis »**chest x-ray:** band atelectasis, elevation of hemidiaphragm, prominent central pulmonary artery, oligaemia at site of embolism	

Common

Pulmonary embolism

History	Exam	1st Test	Other tests
		»**ABG:** hypoxia and hypocapnia are suggestive »**CT pulmonary angiography of chest:** diagnosis is confirmed by direct visualisation of thrombus in a pulmonary artery; appears as a partial or complete intraluminal filling defect »**ventilation-perfusion scan:** normal, low, intermediate, and high probability; pulmonary embolism likely when an area of ventilation is not perfused	

Uncommon

Subdural haematoma

History	Exam	1st Test	Other tests
traumatic event with loss of consciousness, although not always in older patients, who may present more insidiously with headache, lethargy, and/or personality changes	signs of head trauma; normal or focal neurological signs; aphasia is rare	»**CT head:** blood (old and/or new) in subdural space	

Epidural haematoma

History	Exam	1st Test	Other tests
blunt trauma to temporoparietal aspect of skull, classic presentation of loss of consciousness	physical examination may be normal, depending on location, size, and presence or absence of mass effect;	»**CT brain without intravenous contrast:** lenticular/ biconvex hyperdensity	

Uncommon

Epidural haematoma

History	Exam	1st Test	Other tests
followed by period of lucidity and subsequent neurological deterioration; may have headache, vomiting, lethargy	ipsilateral pupillary dilation seen in 30% of cases		

Subarachnoid haemorrhage

History	Exam	1st Test	Other tests
thunderclap or abrupt-onset headache; associated nausea, vomiting, and stiff neck, with or without focal neurological deficits	nuchal rigidity or focal neurological signs may be present	»**CT head:** blood in subarachnoid space May be normal; if normal, LP must be done to establish diagnosis.	»**lumbar puncture:** erythrocytosis or xanthochromia

Brain tumour

History	Exam	1st Test	Other tests
may present with unexplained weight loss, focal neurological deficits, history of cancer; headache that awakens patient from sleep or is present on awakening, decreases after being awake for several hours, is aggravated by exertion or Valsalva	focal neurological deficits	»**CT brain with intravenous contrast:** ring-enhancing lesions with or without surrounding oedema Most brain tumours causing headaches can be seen on non-enhancing contrast CT.	»**MRI brain with and without gadolinium:** ring-enhancing lesion Recommended test after non-enhancing contrast CT if suspicious lesion is noted. May be more sensitive than CT for smaller lesions <2 mm. Drawbacks for unstable patients or patients with claustrophobia; MRI requires longer time in scanner.

Uncommon

Non-convulsive status epilepticus

History	Exam	1st Test	Other tests
typically present with altered consciousness; may also exhibit altered or strange activity, such as facial or limb automatisms, dystonic posturing, and restlessness	neurological examination can be non-focal	»**electroencephalogram:** intermittent or continuous focal or generalised ictal discharges	

Hypertensive encephalopathy

History	Exam	1st Test	Other tests
may be past history of hypertension, use of sympathomimetic drugs or monoamine oxidase inhibitors; dizziness; headache; numbness; weakness; chest pain; shortness of breath	elevated BP, loss of sensation or motor strength, peripheral oedema, new cardiac murmur, elevated jugular venous pressure, rales, oliguria or polyuria, fundoscopic changes associated with hypertensive retinopathy (arteriolar spasm, retinal oedema, retinal haemorrhages, retinal exudates, papilloedema, engorged retinal veins)	»**serum electrolytes, creatinine, urea:** may reveal elevated creatinine »**FBC and smear:** may reveal schistocytes indicating the presence of haemolysis »**urinalysis:** may reveal presence of red cells and protein »**ECG:** may reveal evidence of ischaemia or infarct such as ST- or T-wave changes »**CT head:** may reveal evidence of infarct or haemorrhage »**MRI head:** may reveal evidence of infarct or haemorrhage More sensitive than non-contrast CT scan, but may not be available as first-line investigation in all centres. »**chest x-ray:** may reveal evidence of pulmonary oedema indicating left ventricular failure or	

Uncommon

Hypertensive encephalopathy

History	Exam	1st Test	Other tests
		widened mediastinum indicating possible aortic dissection »**spot urine or plasma metanephrine:** may reveal elevated metanephrine levels May be useful before initiation of drug therapy to rule out phaeochromocytoma.	

Wernicke's encephalopathy (thiamine deficiency)

History	Exam	1st Test	Other tests
most common in people with nutritional deficiency (including alcoholics) or anorexia nervosa, or in professions where excess weight discouraged (e.g., jockeys, ballerinas, models); confusion, confabulation, impaired coordination, double vision	jargon speech, poor comprehension and attention, nystagmus, ophthalmoplegia, ataxia	»**therapeutic trial of parenteral thiamine:** clinical response to treatment	»**serum thiamine level:** low Intravenous thiamine is given on suspicion, before lab tests are done and always before glucose.

Hypercalcaemia

History	Exam	1st Test	Other tests
history of hyperparathyroidism; malignancy, and/or thiazide diuretic use; nausea, vomiting, abdominal pain, constipation, anorexia, increased urination; altered mental status[54]	signs of malignancy on examination; hypertension; hyperreflexia; tongue fasciculations; signs of dehydration (e.g., orthostasis, poor skin turgor)	»**serum calcium:** calcium >2.9 mmol/L (>11.5 mg/dL)	

Uncommon

Hypocalcaemia

History	Exam	1st Test	Other tests
history of neck surgery, muscle cramping; shortness of breath; numbness; abdominal pain	distal-extremity numbness; proximal muscle weakness; Chvostek's sign (tetany); Trousseau's sign (latent tetany); wheezing; bradycardia; stridor	»**serum calcium:** calcium <2.1 mmol/L (<8.5 mg/dL)	»**serum free (ionised) calcium:** calcium <1.0 mmol/L (<4.0 mg/dL) »**ECG:** prolonged QT interval

Carbon monoxide poisoning

History	Exam	1st Test	Other tests
nausea, headache, vomiting, blurred vision, dizziness	cutaneous blistering, tachycardia, hypotension, cardiac arrhythmias, pulmonary oedema, confusion, coma	»**serum carboxyhaemoglobin (CO-Hb) level:** toxic effects appear at 15% to 20%, severe poisoning occurs at 25% Normal levels are around 1% to 3% and in smokers up to 10%. »**serum lactate:** elevated »**cardiac monitoring:** tachycardia, arrhythmias »**ECG:** tachycardia, arrhythmia, or ischaemia/infarction »**chest x-ray:** cardiomegaly, increased pulmonary vasculature, and increased alveolar markings	

Hyperthermia

History	Exam	1st Test	Other tests
may be a history of exercising intensely under hot, humid	generally associated with core temperatures >40°C (>104°F),	»**core temperature measurement:** >40°C (>104°F)	

Uncommon

Hyperthermia

History	Exam	1st Test	Other tests
conditions, or in older adults; central nervous system symptoms such as headache, anxiety, dizziness, irritability, ataxia; nausea/vomiting	although heat stroke can occur at lower core temperatures; increased respiratory rate, flushing, may be diffuse crackles on chest auscultation		

Adrenal insufficiency

History	Exam	1st Test	Other tests
weakness; skin pigmentation; weight loss; abdominal pain; diarrhoea; salt craving; infection; history of corticosteroid use	signs of dehydration, tachycardia, increased respiratory rate, hypotension, rash or darkening of skin	»**serum electrolytes:** high potassium, low sodium »**plasma glucose:** low	»**adrenocorticotropic hormone stimulation test:** low cortisol level

Thyrotoxicosis

History	Exam	1st Test	Other tests
change in appetite, weight loss, anxiety, palpitations, sweating and heat intolerance, oligomenorrhoea, mood change, fatigue	goitre, lid lag, exophthalmos, tachycardia, proximal muscle weakness, tremor; thyroid storm also causes high fever and coma	»**thyroid function tests:** elevated free thyroxine and/or free triiodothyronine; suppressed thyroid-stimulating hormone	»**I-123 thyroid scan and uptake:** may be 'hot' areas in toxic adenoma, diffuse uptake in Graves' disease, or low uptake in thyroiditis

Myxoedema coma

History	Exam	1st Test	Other tests
reduced consciousness, usually in older patient with infection or over-sedation; may also be weight gain, depression, lethargy, feeling cold, forgetfulness, constipation	coma, hypothermia, bradycardia, signs of cardiac and respiratory failure, dry skin, facial and eyelid oedema, thick tongue	»**thyroid-stimulating hormone:** elevated in primary hypothyroidism; may be low, normal, or slightly elevated in central hypothyroidism »**free thyroxine:** low	»**peroxidase antibodies (antithyroid and antimicrosomal):** elevated in primary hypothyroidism Elevated in >90% of patients with autoimmune thyroiditis, the most common

Uncommon

Myxoedema coma

History	Exam	1st Test	Other tests
			cause of primary hypothyroidism.

Pituitary apoplexy

History	Exam	1st Test	Other tests
headache, diplopia, nausea, vomiting, altered mental status, 2:1 male predominance, most commonly seen in ages 37 to 57 years	visual deficits: ptosis, changes in visual field	»**MRI head:** pituitary haemorrhage	»**CT head:** pituitary haemorrhage CT might be easier to obtain quickly, but pituitary haemorrhage might not be seen.

Meningitis

History	Exam	1st Test	Other tests
fever, headache, stiff neck, rarely seizures, older patients present more atypically (afebrile, lethargic)	findings associated with meningeal inflammation: acute fulminant illness, and triad of fever, headaches, and nuchal rigidity; in meningococcaemia, maculopapular rash and/or petechial rash; Brudzinski's sign; Kernig's sign; possible focal neurological deficit[56]	»**lumbar puncture (LP) and culture of cerebrospinal fluid (CSF):** opening pressure >180 mmH2O, elevated WBC count present in CSF, pathogens identified on culture Cranial CT scan should be considered before LP in the presence of focal neurological deficit. »**blood cultures:** recovery of causative organism	

Encephalitis

History	Exam	1st Test	Other tests
initial fever plus malaise followed by speech difficulty, seizures,	cognitive testing demonstrates language disturbance (aphasia,	»**MRI brain:** hyperintensities in the medial temporal lobe	»**FBC:** WBC count reduced, normal, or elevated

Uncommon

Encephalitis

History	Exam	1st Test	Other tests
behavioural changes, impaired alertness; history of overseas travel; history of recent infection with infectious mononucleosis, measles, or rubella; may also experience convulsions	paraphasic errors in speech, anomia, apraxia) and evidence of temporal lobe seizures (staring, unresponsiveness, automatisms); West Nile encephalitis: may have bulbar paralysis and quadriplegia	and insular cortex on one or both sides Given a compatible clinical picture, this is almost diagnostic of herpes simplex encephalitis. Limbic encephalitis (an autoimmune disorder that is often a paraneoplastic syndrome) is considered if only medial temporal lobe structures are involved.	»**cerebrospinal fluid (CSF) analysis:** polymerase chain reaction (PCR) positive for causative virus; usually lymphocytic pleocytosis with elevated protein and normal glucose Prior neuroimaging is wise to exclude significant mass effect, which can make lumbar puncture hazardous. PCR is highly specific and sensitive and is positive in 90% of cases. Diagnosis can be confirmed by finding IgM antibodies for certain viruses (herpes simplex virus, rabies virus, arthropod-borne virus) in the CSF. »**electroencephalogram:** periodic lateralised epileptiform discharges (PLEDs) over one or both temporal lobes PLEDs can be seen in other acute/subacute structural lesions but, given context, are sensitive in >80% of cases of acute herpes simplex encephalitis; can be helpful in monitoring for seizures.

Uncommon

Neurosyphilis

History	Exam	1st Test	Other tests
personality change, gait impairment, incontinence, headache, lightning pains, blurred vision, photophobia, reduced colour perception	hyporeflexia, ataxia, anisocoria, Argyll Robertson pupils, cranial neuropathy, dementia, paranoia	»**cerebrospinal fluid (CSF) examination and Venereal Disease Research Laboratory (VDRL) test:** lymphocytic pleocytosis, elevated protein, reactive VDRL test A positive VDRL test in the CSF is usually considered sufficient to diagnose neurosyphilis.[57]	»**treponemal serological tests:** positive Multiple tests available to measure antibodies to *Treponema pallidum* , including *T pallidum* particle agglutination, enzyme immunoassays, or chemiluminescence immunoassays. Highly sensitive, but not specific: a positive result should be confirmed with rapid plasma reagin or VDRL testing.[57] »**CT or MRI head:** generalised cerebral atrophy with ventricular dilation

Brain abscess

History	Exam	1st Test	Other tests
fever, headache, motor weakness, neck stiffness, vomiting, visual disturbance, seizures, impaired consciousness[58]	pyrexia, hemiparesis, focal neurological abnormalities, septic shock, meningism, papilloedema	»**CT or MRI head:** identification of abscess	»**blood culture:** isolation of pathogens

Mesenteric ischaemia

History	Exam	1st Test	Other tests
chronic recurrent abdominal pain, usually worse after eating (referred to as abdominal angina);	subjective complaint of abdominal pain out of proportion to examination findings; signs of peripheral	»**CT or MRI angiography, or duplex ultrasound of abdomen:** stenosis, thrombus, or reduced	»**abdominal arteriography:** diminished blood flow to the intestine

Uncommon

Mesenteric ischaemia

History	Exam	1st Test	Other tests
may lead to food phobia and weight loss; acute presentation with abdominal pain and bloody diarrhoea may be secondary to acute ischaemic colitis; presence of risk factors for vascular disease, including diabetes, hypertension, renal disease, cardiovascular disease, and/or tobacco abuse	vascular disease may be present, such as diminished peripheral pulses or cool extremities; with severe atherosclerotic disease, an abdominal bruit may be heard	blood flow in the coeliac artery, superior mesenteric artery, or inferior mesenteric artery Specific test if performed by an experienced radiologist.	

Appendicitis

History	Exam	1st Test	Other tests
sudden-onset severe abdominal pain, pain commonly originates near the umbilicus or the epigastrium; often periumbilical with migration to right lower quadrant; nausea, vomiting, anorexia, fever, diarrhoea, more common in children and young adults; pain may improve after rupture	fever, tachycardia, patient may be lying in right lateral decubitus position with hips flexed; no or decreased bowel sounds; right lower quadrant (McBurney's point) tenderness with rigid abdomen; guarding and rebound tenderness; psoas sign (right lower quadrant pain with right thigh extension)	»**abdominal ultrasound:** transverse outer diameter of appendix ≥6 mm Appendix is assessed by graded compression technique. »**FBC:** elevated WBC count (ranging from 10 x 10^9/L to 20 x 10^9/L [10,000 to 20,000 cells/microlitre], >75% neutrophils)	»**CT abdomen:** abnormal appendix (diameter >6 mm) identified or calcified appendicolith seen in association with periappendiceal inflammation

◊ Acute diverticulitis

History	Exam	1st Test	Other tests
persistent left lower quadrant pain; fever, anorexia, nausea, vomiting, abdominal distension (with ileus); patient may have history of diverticulosis	fever, left lower quadrant tenderness, stool blood may be present, may have diffuse tenderness with peritoneal signs (guarding, rebound tenderness, rigid abdomen) with	»**CT abdomen/pelvis with intravenous, oral, and rectal contrast:** may see diverticula, inflammation of pericolonic fat, thickening of the bowel	»**FBC:** elevated WBC count WBC count may be >10 x 10^9/L (10,000 cells/microlitre). »**water-soluble contrast enema:** may see diverticula along

Uncommon

◊ Acute diverticulitis

History	Exam	1st Test	Other tests
	perforation or ruptured abscess	wall, free abdominal air, and an abscess	with extravasation of contrast material into an abscess cavity or into the peritoneum Use of barium enema should be avoided due to risk of barium peritonitis. »**ultrasound:** may see fluid collections around the colon or a thickened hypoechoic bowel wall »**endoscopy:** may see inflamed diverticulum, abscess, and perforation Limited availability in acute setting due to risk of perforation.

◊ Constipation

History	Exam	1st Test	Other tests
altered bowel habits; abdominal pain; pain on defecation	tender abdomen; mass on palpation	»**abdominal x-ray:** dilated loops of bowel; faecal loading in right colon	

Guidelines

United Kingdom

Delirium: prevention, diagnosis and management in hospital and long-term care (https://www.nice.org.uk/guidance/CG103)

Published by: National Institute for Health and Care Excellence
Last published: 2023

North America

Delirium, dementia, and depression in older adults: assessment and care, second edition (http://rnao.ca/bpg/guidelines)

Published by: Registered Nurses Association of Ontario
Last published: 2016

The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease (https://www.alz.org/research/for_researchers/diagnostic-criteria-guidelines)

Published by: National Institute on Aging; Alzheimer’s Association
Last published: 2011

Evidence tables

What are the effects of early versus late initiation of empiric antimicrobial treatment in adults with or at risk of developing sepsis or severe sepsis?[17]

This table is a summary of the analysis reported in a guideline (underpinned by a systematic review) that focuses on the above important clinical question.

View the full source guideline (https://www.nice.org.uk/guidance/ng51/evidence)

Evidence C *	Confidence in the evidence is very low or low where GRADE has been performed and the intervention may be more effective/beneficial than the comparison for key outcomes. However, this is uncertain and new evidence could change this in the future.

Population: Adults with or at risk of developing sepsis or severe sepsis
Intervention: Early initiation of empiric antimicrobial treatment
Comparison: Late initiation of empiric antimicrobial treatment

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
<1 hour versus >1 hour		
Mortality [a]	Favours intervention	Very Low
Mortality - Intensive Care Unit (ICU) setting	Favours intervention	Very Low
Mortality - Emergency Department (ED) setting	No statistically significant difference	Very Low
<2 hours versus >2 hours		
Mortality [a]	No statistically significant difference	Very Low
Mortality - ICU setting	Favours intervention	Very Low
Mortality - ED setting	No statistically significant difference	Very Low
<3 hours versus >3 hours		
Mortality [a]	Favours intervention	Very Low
Mortality - ICU setting	No statistically significant difference	Very Low

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
Mortality - ED setting	Favours intervention	Very Low
<4 hours versus >4 hours		
Mortality - ED setting	No statistically significant difference	Very Low
<5 hours versus >5 hours		
Mortality - ED setting	No statistically significant difference	Very Low
<6 hours versus >6 hours		
Mortality [a]	Favours intervention	Very Low
Mortality - ICU setting	No statistically significant difference	Very Low
Mortality - ED setting	Favours intervention	Very Low

Recommendations as stated in the source guideline

The guideline committee recommends that adults, children, and young people over the age of 12 who have suspected sepsis and one or more high-risk criteria, should be given a broad-spectrum antimicrobial at the maximum recommended dose without delay (within 1 hour of establishing they meet high-risk criteria in an acute hospital setting).[b] See guideline for details on criteria for different levels of risk.

Note

Results in this table are based on observational studies only.

[a] Includes overall mortality in intensive care and emergency department settings.

[b] This guideline recommends that all people with suspected sepsis have a face-to-face assessment and a risk stratification tool is used to determine risk of severe illness and death from sepsis. Recommendations depend on the presence and number of high-, moderate-to-high, and low-risk criteria.

What are the effects of early versus late initiation of empiric antimicrobial treatment in children with or at risk of developing sepsis or severe sepsis?[17]

This table is a summary of the analysis reported in a guideline (underpinned by a systematic review) that focuses on the above important clinical question.

View the full source guideline (https://www.nice.org.uk/guidance/ng51/evidence)

Evidence C *	Confidence in the evidence is very low or low where GRADE has been performed and the intervention may be more effective/beneficial than the comparison for key outcomes. However, this is uncertain and new evidence could change this in the future.

Population: Children with or at risk of developing sepsis or severe sepsis
Intervention: Early initiation of empiric antimicrobial treatment
Comparison: Late initiation of empiric antimicrobial treatment

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
<1 hour versus >1 hour [a]		
Paediatric Intensive Care Unit (PICU) mortality	No statistically significant difference	Very Low
<2 hours versus >2 hours [a]		
PICU mortality	No statistically significant difference	Very Low
<3 hours versus >3 hours [a]		
PICU mortality	Favours intervention	Very Low
<4 hours versus >4 hours [a]		
PICU mortality	Favours intervention	Very Low

Recommendations as stated in the source guideline
The National Institute of Health and Care Excellence (NICE) 2016 guideline on Sepsis: recognition, diagnosis and early management makes the following recommendation:

For children aged 5–11 years who have suspected sepsis and 1 or more high-risk criteria, give a broad-spectrum antimicrobial [b] at the maximum recommended dose without delay (within 1 hour of identifying that they meet any high-risk criteria in an acute hospital setting).

Note
The guideline group noted that the direct evidence in children came from one small (n=130), single-centre retrospective study of children in PICU with severe sepsis and septic shock. Therefore, they also

extrapolated from the indirect evidence in adults to make the same recommendation for all age groups (including children aged under 5 years and 5-11 years).

[a] Time from sepsis recognition to initial treatment and first appropriate treatment.

[b] See full guideline for more information.

* Evidence levels

The Evidence level is an internal rating applied by BMJ Best Practice. See the EBM Toolkit (https://bestpractice.bmj.com/info/evidence-tables/) for details.

Confidence in evidence

A - High or moderate to high

B - Moderate or low to moderate

C - Very low or low

† Effectiveness (BMJ rating)

Based on statistical significance, which demonstrates that the results are unlikely to be due to chance, but which does not necessarily translate to a clinical significance.

‡ Grade certainty ratings

High	The authors are very confident that the true effect is similar to the estimated effect.
Moderate	The authors are moderately confident that the true effect is likely to be close to the estimated effect.
Low	The authors have limited confidence in the effect estimate and the true effect may be substantially different.
Very Low	The authors have very little confidence in the effect estimate and the true effect is likely to be substantially different.

BMJ Best Practice EBM Toolkit: What is GRADE? (https://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/)

Key articles

- American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th ed., text revision (DSM-5-TR). Washington, DC: American Psychiatric Publishing; 2022.
- Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med. 2021 Nov 1;49(11):e1063-143. Full text (https://www.doi.org/10.1097/CCM.0000000000005337) Abstract
- McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011 May;7(3):263-9. Full text (https://www.doi.org/10.1016/j.jalz.2011.03.005) Abstract

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Please note that recommended formulations and doses may differ between drug databases drug names and brands, drug formularies, or locations. A local drug formulary should always be consulted for full prescribing information.

Treatment recommendations in BMJ Best Practice are specific to patient groups. Care is advised when selecting the integrated drug formulary as some treatment recommendations are for adults only, and external links to a paediatric formulary do not necessarily advocate use in children (and vice-versa). Always check that you have selected the correct drug formulary for your patient.

Where your version of BMJ Best Practice does not integrate with a local drug formulary, you should consult a local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing before prescribing.

Interpretation of numbers

Regardless of the language in which the content is displayed, numerals are displayed according to the original English-language numerical separator standard. For example 4 digit numbers shall not include a comma nor a decimal point; numbers of 5 or more digits shall include commas; and numbers stated to be less than 1 shall be depicted using decimal points. See Figure 1 below for an explanatory table.

BMJ accepts no responsibility for misinterpretation of numbers which comply with this stated numerical separator standard.

This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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