The unconscious patient

Tim Cooksley
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Abstract
The unconscious patient is a medical emergency which can challenge the diagnostic and management skills of any clinician. A systematic and logical approach is necessary to make the correct diagnosis; the broad diagnostic categories being neurological, metabolic, diffuse physiological dysfunction and functional. Even when the diagnosis is not immediately clear, appropriate measures to resuscitate, stabilize and support an unconscious patient must be performed rapidly. The key components in the assessment and management of a patient, namely history, examination, investigation and treatment, are performed in parallel, not sequentially. Unless the cause of unconsciousness is immediately obvious and reversible, help from senior and critical care colleagues will be necessary. In particular, senior help will be needed to make difficult management decisions in patients with a poor prognosis.

Keywords acute brain injury; alcohol intoxication; coma; diabetic coma; drug intoxication; metabolic emergencies; neurological emergencies; post-ictal; stroke; unconscious

Definition

Unconsciousness or coma is defined as a sleep-like state, due to a diverse range of aetiologies and pathologies, from which the patient cannot be aroused.[1] The patient is completely unaware and unresponsive to external stimuli, with the exception of motor responses such as eye opening and/or limb withdrawal to painful stimuli.[2]

Pathophysiology of an unconscious patient

The pathophysiology of an unconscious patient is complex. It is caused by two primary mechanisms. The first of these is a diffuse insult to both cerebral hemispheres. The second mechanism is a disruption of the ascending reticular activating system in the midbrain and pons, where signals are carried to the thalamus and cortex. The thalamus plays a crucial role in maintaining arousal. The thalamus and ascending reticular activating system can be damaged either by direct insult or by problems arising within the brainstem.[2]

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Differential diagnosis of an unconscious patient

The most likely diagnoses in an unconscious patient are shown in Table 1. They can be categorized as:

- neurological — due to either structural injury of the cerebral hemispheres, direct injury to or extrinsic compression of the brainstem
- metabolic — usually an acute metabolic or endocrine derangement (e.g. hypoglycaemia)
- diffuse physiological brain dysfunction (e.g. intoxication with alcohol, drug overdose, seizures or hypothermia)
- psychiatric — a functional as opposed to an organic cause.

Assessment of the unconscious patient

The clinical approach to an unconscious patient should be structured. Figure 1 outlines a management algorithm. By necessity, it requires the clinician to deviate from the traditional sequential approach of history, examination, investigation and management[1]; instead, all four components can and should proceed in parallel through a team approach. Below, we consider the important aspects of each of the four domains in the traditional order.

Key components of the history

Unconscious patients by definition cannot give a history. Gaining a collateral history from relatives or other witnesses to the event that preceded admission, or from the paramedics who attended the patient, may provide vital clues as to the aetiology of the condition.[1] This can and should be done simultaneously whilst managing the patient.

Important aspects of the history include recent symptoms or illnesses, significant previous medical history, recent surgery or treatments and a medication history. An understanding of the patient's existing functional status and pre-morbid condition is important; it will help inform decisions regarding escalation of care and whether admission to intensive care and cardiopulmonary resuscitation are appropriate. Urgent review of the patient's previous medical notes and results may also provide essential clues.

Paramedic teams or bystander witnesses may notice additional clues, such as used syringes or evidence of other recreational drug use, alcohol, empty medication packets or a suicide note. The paramedics are likely to have instituted pre-hospital treatments; it is important to ascertain the patient's response to these and to enquire about their conscious state at the scene to assess whether they are more or less responsive when reviewed.

Clinical examination of the unconscious patient

Determining unresponsiveness: initially the patient will have their eyes closed with a lack of facial expression and will be oblivious to environmental stimuli.[3] A stepwise approach evaluates response to graded stimuli[3]:

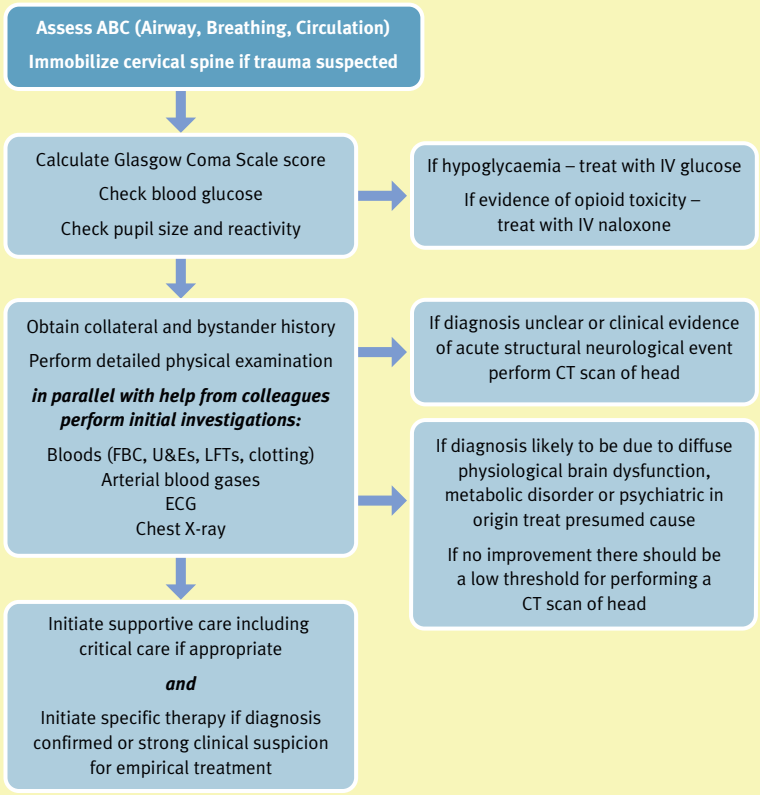
- *Verbal stimulus* — 'Can you hear me?' or 'Are you OK?'
- *Tactile stimulus* — to either the hands or face.

Differential diagnoses in an unconscious patient[2]

Neurological	Metabolic	Diffuse physiological brain dysfunction	Psychiatric
Ischaemic stroke	Hypoglycaemia	Seizures	Psychiatric coma
Intracerebral haemorrhage	Hyperglycaemia	Alcohol intoxication	Malingering
Subarachnoid haemorrhage	Hyponatraemia	Opioid toxicity	
Subdural haematoma	Hypernatraemia	Drug overdose	
Brain tumour	Hypercalcaemia	Poisoning	
Cerebral lymphoma	Addisonian crisis	Hypothermia	
Multiple brain metastases	Hypothyroidism	Neuroleptic malignant syndrome	
CNS infection	Uraemia		
Cerebral abscess	Hypercapnia		
Cerebral oedema	Septic encephalopathy		
Hydrocephalus			
Posterior reversible encephalopathy syndrome			
Trauma			

Table 1

Algorithm for initial management of the unconscious patient



- *Noxious stimulus* — these should be intense but not cause injury. Pressure on the supra-orbital ridge or nail-bed pressure are appropriate examinations.

Neurological assessment: initial neurological examination focuses on determining the level of consciousness using the Glasgow Coma Scale (GCS) score (Table 2).

Assessment of the cranial nerves and motor response to pain should be performed. Pupil examination can provide useful clues as to the aetiology:[2]

- *small pupils (<2 mm)* — can be due to either opioid toxicity or a pontine lesion
- *midsize pupils (4–6 mm) unresponsive to light* — can be due to a midbrain lesion
- *maximally dilated pupils (>8 mm)* — can be due to drug toxicity (amphetamines, cocaine) or an oculomotor nerve pathology
- *unilateral fixed pupil* — due to a third cranial nerve lesion.

Motor function is assessed by noxious stimuli as described above. It is important to distinguish between purposeful and reflexive responses.[3] Purposeful responses include the patient following commands, pushing the examiner away, localizing to the noxious stimulus and reaching for airway adjuncts. Reflexive responses are withdrawal, flexion or extension to the stimulus.

Fundoscopy may reveal key diagnostic findings, for example papilloedema in patients with hypertensive crisis and posterior reversible encephalopathy syndrome (PRES; see below), or subhyaloid haemorrhage in patients with subarachnoid haemorrhage.

General physical examination: doctors with a sensitive sense of smell may recognize the musty smell of hepatic encephalopathy or the garlic smell associated with organophosphate poisoning.[4] Whilst alcohol may also be smelt on the breath of an unconscious patient, it is strongly recommended that all unconscious patients who appear to be intoxicated are fully assessed for other causes of unconsciousness, the alcohol may be masking the true cause of unconsciousness, for example a head injury. Look for potential drug injection sites (groins, arms) or sites for subcutaneous insulin injections.

Breathing pattern abnormalities can provide useful clues:

- Cheyne–Stokes breathing can occur with many underlying pathologies and is not helpful in differentiating between diagnoses in the unconscious patient.
- Ataxic breathing (Biot's respiration) is an abnormal pattern of breathing, characterized by groups of quick, shallow inspirations followed by regular or irregular periods of apnoea, and indicates a lesion in the lower pons.[5]
- Central neurogenic hyperventilation is an abnormal pattern of breathing, characterized by deep and rapid breaths at a rate of at least 25 breaths per minute, and indicates a lesion in the pons or midbrain.[6]

Investigations

- Blood glucose
- Urea and electrolytes
- Calcium
- Liver function tests
- Clotting screen
- Toxicology screen, including paracetamol and salicylate concentrations
- ECG
- Chest X-ray

In addition, for patients with fever or features of sepsis, blood cultures should be taken and arterial blood gases considered. Urgent imaging of the brain is extremely important, especially if the cause of the coma is unclear; if the cause of coma is not obvious from the initial rapid assessment a structural pathology should be considered.[1,2] A head and brain computed axial tomogram (CT) is the initial imaging modality of choice to exclude common pathologies such as subarachnoid haemorrhage, subdural haematoma, stroke or mass lesions. Common abnormalities seen on CT imaging are listed in Table 3. If CT imaging of the brain is normal and the diagnosis remains unclear then further imaging with a magnetic resonance scan may be needed depending on clinical circumstances.

The Glasgow Coma Scale

Eye opening	Movement	Verbal
4 — Spontaneous	6 — Obeys commands	5 — Oriented
3 — To speech	5 — Localizes to pain	4 — Confused
2 — To pain	4 — Withdraws from pain	3 — Inappropriate words
1 — None	3 — Abnormal flexion to pain	2 — Incomprehensible sounds
	2 — Extensor response to pain	1 — None
	1 — No response	

Table 2

Basic CT scan findings of key neurological conditions that may be seen in an unconscious patient

Disease process	CT scan findings
Subarachnoid haemorrhage	Haemorrhage into CSF spaces (cisterns, convexity). Complicated by hydrocephalus in about 20% of cases. 98% sensitive at 12 hours after onset of symptoms
Subdural haematoma	Sickle- or crescent-shaped collection of blood (usually over the convexity). Can be either acute or chronic
Ischaemic stroke	The earliest change seen is a loss of grey–white matter differentiation at the site of ischaemia
Tumour	Hypodense lesion. Usually surrounded by oedema (due to a loss of the integrity of the blood–brain barrier allowing fluid to pass into the extracellular space)
Hydrocephalus	Dilatation of the ventricles
PRES	Classically vasogenic oedema of the bilateral parietal–occipital lobes. Usually symmetrical. A significant proportion have atypical findings

Table 3

Lumbar puncture: in the absence of a contraindication, there should be a low threshold for performing a lumbar puncture, especially when the diagnosis of the coma is unclear and/or there is a suspicion of a central nervous system infection. The key components of a lumbar puncture are:

- measurement of the opening pressure
- description of the CSF appearance (colour, turbidity, blood-stained)
- CSF analysis:
  - cell count (white cell count and red cell count)
  - Gram stain
  - glucose (with a contemporaneous plasma glucose)
  - protein
  - culture
  - consider sending samples for polymerase chain reaction (PCR) testing and viral titres, India ink staining and cryptococcal antigen depending on the clinical situation.[7]

Management of the unconscious patient

Every unconscious patient is in a potentially life-threatening situation. Initial management should be performed in parallel with the assessments already discussed.

The ABC (Airway, Breathing, Circulation) approach should be used. If there is a history or suspicion of trauma, the cervical spine should be immobilized. Intubation should be considered in patients who cannot protect their own airway or any unconscious patient with ineffective respiratory drive and poor oxygenation. A GCS score of 8 or less should prompt consideration of the need for airway protection.

Whilst the ABC assessment is taking place, colleagues need to be establishing intravenous access, connecting cardiac and oxygen saturation monitoring and starting oxygen therapy if indicated. Hypotension should be treated with intravenous fluid resuscitation initially, but with consideration of inotropic support if the blood pressure does not respond.

Specific therapies: treatment depends on the underlying aetiology. In cases where there is clinical suspicion of toxicity, specific antidotes should be used:

- *Hypoglycaemia* — must always be excluded. If present it should be monitored and treated with an intravenous (IV) infusion (over 10–15 minutes) of glucose 20% 75–80 ml or glucose 10% 150–160 ml.[8] Glucagon (1 mg intramuscularly (IM)) can be used but can take up to 15 minutes to act and is ineffective in patients with liver disease, depleted glycogen stores or malnutrition.[8] Co-administration of intravenous thiamine should be considered in all patients felt to be at risk of Wernicke's encephalopathy,[1] for example alcoholics. If a patient presents with hypoglycaemia it is essential to determine whether they have diabetes mellitus. If so, what is their normal medication? If not, liver disease, overdose, Addison's disease and malnutrition should be considered.
- *Opioid toxicity* — administration of naloxone (0.4–2 mg IV). Naloxone is a competitive opioid antagonist and the dose required depends upon the amount of opioid taken. Relapse is common as naloxone has a short half-life (20–30 minutes) and recurrent injections or an infusion may be required.[9] Naloxone can be used IV, IM or intranasally.[10]
- *Benzodiazepines* — administration of IV flumazenil can be considered in confirmed benzodiazepine toxicity. However, it is contra-indicated in patients with a history of seizures and in concomitant tricyclic overdose it may provoke seizures.
- *Severe hyponatraemia* — is a complex condition and, in the unconscious patient, should be managed by experts in a critical care setting. It is important to assess whether the hyponatraemia is acute or chronic and, unless the patient is having seizures, to correct it gradually to avoid central pontine myelinolysis.
- *Hypercalcaemia* — if symptomatic, the first-line therapy is IV sodium chloride 0.9%; thereafter, calcitonin, IV bisphosphonates and IV glucocorticoids can be considered depending on the serum calcium, the underlying cause and the response to sodium chloride 0.9%.[11]
- *Toxicity with methanol, lithium, salicylate or ethylene glycol* — renal replacement therapy, such as haemofiltration, may be required.

Treatment of the unconscious patient with a neurological cause

In unconscious patients with an acute neurological condition, urgent discussion with neurosurgeons or and neurologists is necessary to determine further management.

If bacterial meningitis is suspected, empirical antibiotic treatment should be commenced pending a lumbar puncture; if encephalitis is suspected, intravenous aciclovir should be given as soon as possible.[7]

PRES is a combined clinical and radiological syndrome characterized by headaches, encephalopathy, seizures and visual loss.[12] It is associated with accelerated hypertension, pregnancy, sepsis and chemotherapeutic agents.[13] Management is aimed at controlling blood pressure, and controlling seizures with IV anticonvulsants and withdrawal of trigger agents.[12,13]

Prognosis of the unconscious patient

The outcome and prognosis of the unconscious patient is determined by the underlying cause. Patients not responding to initial treatment, and who remain unconscious, are likely to require critical care admission unless withdrawal of treatment and palliation of symptoms is appropriate, for example a patient with a catastrophic brain injury.

Summary

Treating an unconscious patient can be a daunting prospect for clinicians. A structured approach focussing on key principles ensures that stabilization of the patient, early diagnosis and appropriate initial management can be achieved. Management is adapted to the underlying cause of the clinical presentation. ◆

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Practice points

- The unconscious patient is a medical emergency
- The components of a traditional patient assessment should be performed in parallel, not sequentially
- Physicians need to be familiar with the common causes of unconsciousness, neurological, metabolic, diffuse physiological dysfunction or functional
- Even if the diagnosis is not immediately obvious, appropriate steps to support the patient should be implemented
- Involvement of critical care colleagues should be sought at an early stage if the cause of unconsciousness is not immediately reversible

Stroke

Keith W Muir

Abstract

Acute stroke and transient ischaemic attack (TIA) are focal neurological syndromes of vascular origin and should be treated as medical emergencies. Brain imaging with computed tomography or magnetic resonance imaging is required to identify ischaemia from haemorrhage, recognize non-stroke pathologies that mimic stroke and guide investigation for underlying mechanism. Acute interventions of benefit in ischaemic stroke include intravenous thrombolysis with alteplase given within 4.5 hours of onset, stroke unit care and aspirin. Decompressive hemicraniectomy reduces mortality in ischaemic stroke complicated by severe brain swelling. Intracerebral haemorrhage accounts for 10% of strokes, and while specific treatments are lacking at present, patients benefit from general measures, notably stroke unit care. Transient ischaemic attack carries a high short-term risk of stroke, and immediate investigation and institution of secondary preventative treatment prevents a high proportion of these events. Secondary prevention for ischaemic stroke and TIA should be tailored according to mechanism in the individual patient and includes anti-platelet therapies, blood-pressure-lowering, statins, carotid endarterectomy and anticoagulation.

Keywords acute treatment; cerebrovascular disease; intracerebral haemorrhage; prevention; stroke

What's new?

- Thrombolysis with IV alteplase improves the likelihood of full recovery when given up to 4.5 hours after onset of ischaemic stroke
- Intravenous thrombolysis is beneficial in elderly patients (>80 years)
- Short-term risk of stroke after transient ischaemic attack (TIA) is high
- Immediate secondary preventative treatment after TIA avoids a high proportion of strokes
- Newer oral anticoagulant drugs offer alternatives to warfarin

Definition

Stroke is a clinical syndrome defined by acute neurological deficit (usually focal) with a vascular basis. Around 85–90% of strokes are ischaemic (resulting from arterial occlusion), and 10–15% result from intracerebral haemorrhage (ICH). The 1976 WHO definition also covers subarachnoid haemorrhage, but this is primarily of epidemiological interest. The term 'transient ischaemic attack' (TIA) conventionally denotes complete resolution of all symptoms within 24 hours, but this arbitrary time limit is probably an anachronism in light of modern imaging and thrombolytic treatment, and there are proposals that TIA be redefined as symptoms of less than 1 hour without brain infarction on magnetic resonance imaging (MRI).[1] The 24-hour duration is used in the studies discussed throughout this article.

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Epidemiology

Stroke incidence increases with age, although a quarter occur in patients under age 65. Causes vary by age group. Ischaemic stroke is the most common, with TIA next and ICH least common.[2] There are approximately 150,000 incident strokes annually in the UK, and globally stroke is the third most common cause of death and the most common disabling neurological disease.

Risk factors

Major predisposing factors for ICH and ischaemic stroke are listed in Table 1. It is important to investigate the underlying mechanism in most individuals, regardless of risk factors.

Diagnosis and natural history

The clinical features of ICH and ischaemic stroke are similar, and the two cannot be distinguished reliably without brain imaging.

Symptoms are of sudden onset and usually maximal in severity at, or within minutes of, onset. Evolution of new neurological deficits or reduced level of consciousness is uncommon within the first few hours, except in expanding ICH and basilar artery occlusion, but some deficits fluctuate dramatically in severity, notably lacunar strokes ('capsular warning syndrome') or incipient carotid occlusion.

Symptoms of TIA are identical to those of ischaemic stroke but can include transient monocular blindness. TIA is distinguished only by complete resolution, typically within 30–60 minutes: the longer the symptoms last, the higher the probability of brain infarction (50% of TIAs resolving within 24 hours have infarcts on diffusion-weighted MRI (DWI)).[3]

Clinical features

Common clinical patterns are summarized by the Oxfordshire Community Stroke Project (OCSP) classification (Figure 1).[4]

Contralateral hemiparesis may involve face, arm and leg equally (internal capsule or corticospinal tract) or be more focal (motor cortex), often face and arm-predominant (middle cerebral artery (MCA) cortical territory) (Figure 2). Hemisensory disturbance is similarly distributed. Restricted motor or sensory deficits

Major risk factors for stroke

Modifiable	Unmodifiable
Intracerebral haemorrhage	
Hypertension	Age
Alcohol excess	Apolipoprotein E ε2 or ε4 carriage (CAA)
Drug treatments — thrombolytic agents, anticoagulants, anti-platelet agents	Race (probably higher in SE Asians)
Diabetes	
Cigarette smoking	
Ischaemic stroke	
Hypertension	Age
Diabetes	
Ischaemic heart disease	
Atrial fibrillation	
Valvular heart disease	
Cigarette smoking	

Table 1

that may mimic peripheral nerve palsies are increasingly recognized with sensitive brain imaging. Severity of weakness is not of itself a reliable indication of stroke severity or prognosis.

Conjugate gaze deviation (away from the affected limbs) results from involvement of the frontal eye field, a bilaterally represented centre that directs voluntary gaze. Often incorrectly attributed to 'neglect', it usually resolves over days. Occasionally, pontine lesions cause gaze deviation towards the affected side.

Higher cortical dysfunction is represented by language disorder (dysphasia) in dominant (usually left) hemisphere MCA strokes, or visuospatial neglect, usually in non-dominant (right) hemisphere strokes. Dysphasia may conform to Broca's syndrome (characterized by non-fluent speech, recognized to be difficult and generally frustrating for the patient, with words omitted or substituted) or Wernicke's syndrome (fluent speech of abnormal content including word or phonemic substitution, the patient generally appearing unconcerned or unaware of the problem) but is often mixed. Broca's pattern dysphasia is usually accompanied by brachiofacial weakness since the relevant brain regions are anatomically close, while Wernicke's pattern dysphasia is usually not accompanied by motor deficits, and thus if often described as 'confusion'. Visuospatial neglect is identified by failure to recognize bilateral simultaneous stimuli (tactile or

Oxfordshire Community Stroke Project (OCSP) classification: syndromes and imaging examples

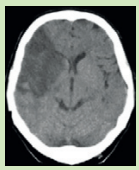
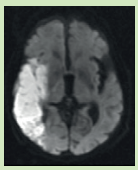
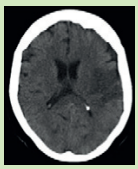
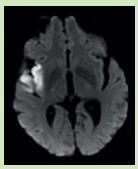
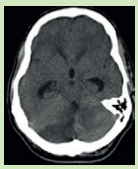
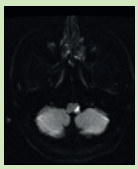
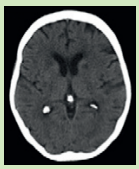
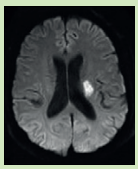
OCSP term	Clinical features	Vascular basis	Example CT	Example MRI
Total Anterior Circulation Syndrome (TACS)	• Hemiparesis **AND** • Higher cortical dysfunction (dysphasia or visuospatial neglect) **AND** • Homonymous hemianopia	Usually proximal middle cerebral artery (MCA) or ICA occlusion		
Partial Anterior Circulation Syndrome (PACS)	• Isolated higher cortical dysfunction **OR** • Any two of hemiparesis, higher cortical dysfunction, hemianopia	Usually branch MCA occlusion		
Posterior Circulation Syndrome (POCS)	• Isolated hemianopia (posterior cerebral artery (PCA)) brainstem or cerebellar syndromes	Occlusion of vertebral, basilar, cerebellar or PCA vessels		
Lacunar Syndrome (LACS)	• Pure motor stroke **OR** • Pure sensory stroke **OR** • Sensorimotor stroke **OR** • Ataxic hemiparesis **OR** • Clumsy hand-dysarthria	Small penetrating artery occlusion, usually in lenticulostriate branches of MCA, or supply to brainstem or deep white matter		

Figure 1

Anterior circulation vascular territories and major intracranial vessels

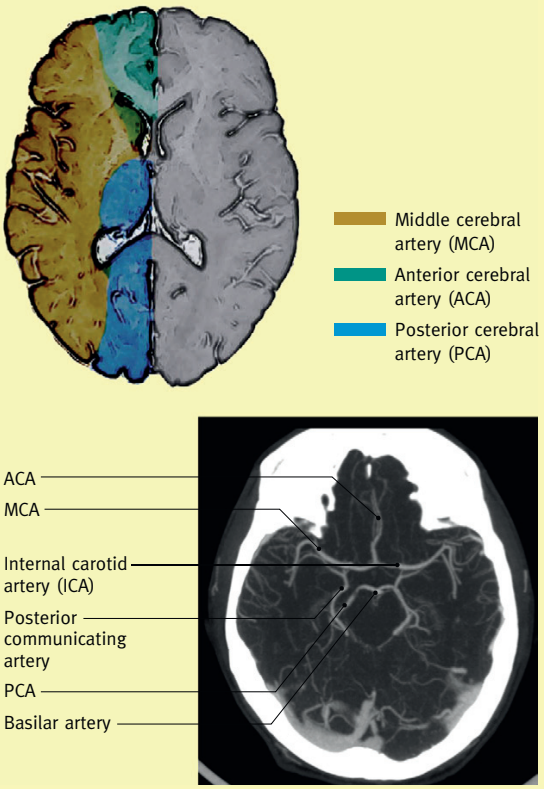


Figure 2

visual) when a unilateral stimulus is perceived and may also manifest as an apraxia of eye opening, unawareness of the neurological deficit (anosognosia) and inability to recognize the affected side.

Contralateral homonymous hemianopia may occur in MCA strokes involving the optic radiation or in isolation with posterior cerebral artery strokes, when late presentation is common since the deficit is commonly asymptomatic or non-specific. Transient monocular blindness is a symptom of retinal ischaemia in ocular TIA.

Differential diagnosis

Common stroke mimics include:

- hypoglycaemia
- migraine aura
- focal seizure or post-ictal state (Todd's paresis)
- brain tumours
- subdural haematoma
- metabolic disturbance (including hypoxia, drug overdose)
- hypotension.

Reduced conscious level is the most important predictor of non-stroke pathology. Stroke rarely causes reduction of conscious level in the first few hours, exceptions being rapidly expanding supratentorial ICH or with bilateral thalamic ischaemia ('top of the basilar' syndrome). In occlusion of the basilar artery (the main blood supply to the brainstem), a patient may be 'locked in' rather than truly unconscious. In non-dominant hemisphere stroke, apraxia of eye opening may lead to a spuriously reduced Glasgow Coma Scale score. Reduced consciousness in ischaemic stroke otherwise typically occurs 2–5 days after onset in large infarcts consequent to brain swelling (sometimes causing the 'malignant MCA syndrome').

In someone with previous stroke, decompensation of an existing deficit may be precipitated by any intercurrent illness, alcohol or sedative medication (which should be actively pursued and treated), stress or tiredness.

Prognosis

Outcome of acute stroke is predicted by the severity of the initial stroke (e.g. using a scoring system such as the National Institutes of Health Stroke Scale, Table 2), age and acute phase blood glucose. Compared to ischaemic stroke, ICH carries higher mortality (50% by day 30 compared to 17%). Outcome is a function of haematoma volume and is worse with early expansion and intraventricular extension of bleeding.

Urgent evaluation of TIA is required since the 30-day stroke risk is around 10%, mainly within the first 7 days. Prognostic scores based on duration, symptoms, age and premorbid conditions may aid risk stratification, and imaging findings including the presence of recent brain ischaemia on diffusion-weighted MRI, intracranial vessel occlusion, or extracranial carotid stenosis, also predict those at highest risk of early stroke.[5]

Investigation

In addition to general assessments (blood pressure, electrocardiography (ECG), biochemistry, blood glucose, cholesterol, full blood count and erythrocyte sedimentation rate (ESR)), specific investigations are required to define pathology and stroke mechanism, informed by the patient's age.

National Institutes of Health Stroke Scale items

Item	Score range
• Level of consciousness (LOC)	0–3
○ LOC questions	0–2
○ LOC commands	0–2
• Best gaze	0–2
• Visual fields	0–3
• Facial weakness	0–3
• Motor arm	0–4 (right and left)
• Motor leg	0–4 (right and left)
• Limb ataxia	0–2
• Sensory loss	0–2
• Best language	0–3
• Dysarthria	0–2
• Extinction and inattention	0–2

Table 2

Most ischaemic strokes result from thromboembolism originating in extracranial vessels or the heart (Figure 3). Intracerebral small vessel disease may give rise to ischaemic strokes or to ICH. Uncommon causes, including inherited disorders, should be considered at any age when a conventional basis is not found. When seeking uncommon causes, structural imaging of heart and intracranial vessels is important and blood tests alone rarely identify a mechanism.

In ICH, haematoma location and patient age offer clues to aetiology (Figure 3), but these associations overlap. Cerebral amyloid angiopathy (CAA) may give rise to repeated bleeding episodes. Arteriovenous malformation (AVM) may underlie ICH, particularly in young or normotensive patients.

Brain imaging is required to confirm the diagnosis and gives insight into mechanism and prognosis. Computed tomography (CT) is sensitive and specific for acute ICH (high attenuation on unenhanced CT). In moderately severe supratentorial acute ischaemic stroke, CT sensitivity is around 66% in the first 5 hours after onset. Radiological signs may be subtle, but have high specificity. Training and a systematic approach to CT review improve recognition.[6]

MRI offers improved sensitivity for both acute ischaemia and chronic haemorrhage compared to CT, but acquisition times are longer with more contraindications. DWI is highly sensitive to acute ischaemia and is more sensitive than CT for small lesions associated with minor or transient deficits.[7] Susceptibility-weighted or gradient echo MRI sequences are sensitive to haemoglobin degradation products and have similar sensitivity to CT for acute ICH, but also identify old haemorrhage, which cannot be distinguished from old ischaemic lesions by CT. The significance of small focal areas of old haemorrhage (cerebral microbleeds) on MRI is under investigation. Multiple microbleeds may support a diagnosis of CAA, depending upon distribution.

Other investigations may be determined by the patient's condition, but will be required in most cases.

Ischaemic stroke

Extracranial vascular imaging for detection of carotid stenoses can be done using duplex ultrasound, CT angiography (CTA) or magnetic resonance angiography (MRA). All have similar sensitivity and specificity compared to catheter angiography. Ultrasound is widely used but its sensitivity for 50% stenosis is not established. CTA or MRA have superior anatomical coverage (including aortic arch, vertebral arteries and intracranial vessels) and may identify atherosclerotic plaque composition or other pathologies such as arterial dissection that ultrasound cannot.

Extended periods of ambulatory ECG monitoring (up to 7–10 days) increase detection of paroxysmal atrial fibrillation compared to single 12-lead recordings. Trans-thoracic echocardiography may identify left ventricular hypertrophy or dysfunction, which may influence secondary prevention decisions, but trans-oesophageal echocardiography is superior for detecting embolic sources related to the left atrial appendage and interatrial septum as well as the aortic arch. Transcranial Doppler ultrasound is an alternative means of identifying large right-to-left shunts, which are more prevalent in young cryptogenic stroke patients.

Intracerebral haemorrhage

Aetiological investigation is often best deferred until after resolution of mass effect from the acute haematoma. Catheter angiography remains the gold standard for vascular imaging, but MRI- and CT-based imaging may be diagnostic. Susceptibility-weighted MRI may identify cavernomas (that are not linked to the vascular system) or suggest CAA.

Treatment

Intracerebral haemorrhage

Neither haemostatic treatment nor active blood-pressure-lowering has been established to improve outcome and trials are on-going. Evidence for acute surgical interventions (evacuation via craniotomy, drainage via burr hole or stereotaxy, external ventricular drainage of intraventricular blood) is limited. A strategy of ICH evacuation within 48 hours was no better than

Intracerebral haemorrhage appearance, location and associations

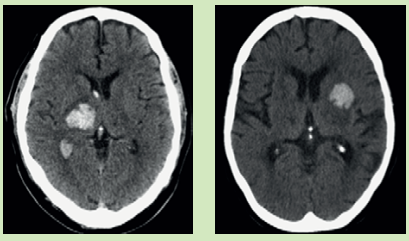
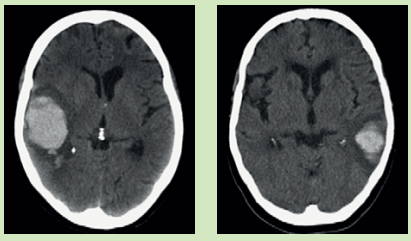
	Deep (55%)	Lobar (33%)
CT examples		
Age	< 75 years	> 75 years
Associations	Hypertension	Cerebral amyloid angiopathy (CAA)

Figure 3

initial conservative management,[8] but few studies have evaluated intervention within the first few hours when deterioration usually occurs. Underlying AVMs may be treated by surgical excision, endovascular occlusion or radiosurgery, depending upon anatomy and local expertise.

Ischaemic stroke

Intravenous thrombolysis with alteplase, a recombinant tissue plasminogen activator, improves the proportion of patients with complete neurological recovery when given within 4.5 hours of symptom onset (absolute benefit 12%, number needed to treat (NNT) 8).[9] Earlier treatment is associated with greater likelihood of benefit.[10] The risk of ICH with significant neurological deterioration is around 2% (higher for asymptomatic ICH) and there is a slightly higher early mortality with treatment[11] but overall benefit remains. The third International Stroke Trial (IST-3) confirmed benefit in a predominantly elderly population previously under-represented in clinical studies.[11] With redesign of acute care systems to facilitate rapid assessment, thrombolysis for 15–20% of ischaemic stroke patients may be possible, and the rapid assessment and scanning of all patients has general benefits.

Intravenous alteplase recanalizes occluded arteries in around 56% of patients, and is least effective in the largest clots (and most severe strokes). Alternative approaches including different thrombolytic drugs, and intra-arterial thrombectomy devices, are being investigated, but at present have not been shown to be superior to alteplase. Thrombectomy may offer an alternative approach in patients with a contraindication to thrombolysis.

Stroke unit care reduces death and dependence significantly (absolute benefit 5%, NNT 20). The specific components of specialized care that confer benefit are incompletely understood, but physical location on a specialist unit is superior to care by mobile teams,[12] and therefore nursing care is likely to be a major factor. Multidisciplinary team involvement, swallowing assessment, fluids, early mobilization and management protocols to correct physiological derangements (hypoxia, hyperglycaemia and pyrexia) are important.

Decompressive hemicraniectomy reduces mortality in patients aged 55 years and younger with malignant brain swelling after large infarction, irrespective of hemisphere involved,[13] but a high proportion of survivors remain disabled.

Aspirin started within 48 hours (300 mg/day for up to 14 days) reduces death or dependence, probably acting as acute secondary prevention. If IV thrombolysis is given, aspirin should be withheld for 24 hours as it increases the risk of haemorrhage.

Rehabilitation is the key to maximizing recovery from acute stroke. Early multidisciplinary team management is essential. Stroke patients are vulnerable to pneumonia, deep vein thrombosis, urinary tract infection, aspiration, depression, falls and shoulder subluxation, as well as coronary artery disease. Any deterioration should prompt review for systemic causes.

Secondary prevention

Preventative treatment should be informed by the mechanism of stroke in each individual.

General measures that lack specific evidence include smoking cessation, glycaemic control in diabetes or impaired glucose tolerance, weight reduction and exercise.

Significantly fewer strokes occurred when secondary preventative treatments were started within 24 hours of symptoms in patients with TIA, compared to delayed institution of treatment, in non-randomised comparisons.[14,15]

Anti-platelet treatment

The combination of aspirin (75 mg daily) and dipyridamole modified release (200 mg 12-hourly) is superior to aspirin monotherapy, but dipyridamole causes headache in 6% and may not be tolerated. Clopidogrel monotherapy appeared equivalent to aspirin–dipyridamole in one large trial.[16]

Blood-pressure-lowering treatment

In addition to controlling high blood pressure, lowering blood pressure in individuals considered 'normotensive' reduced stroke and cardiovascular events in the PROGRESS trial and should be considered in haemodynamically stable patients unless there is bilateral severe carotid stenosis.[17]

Statins

Simvastatin and atorvastatin reduce stroke and other cardiovascular events after stroke or TIA. The small effect size may reflect different benefits according to stroke mechanism. A reported increased risk of ICH with high-dose atorvastatin was predominantly seen in patients with previous haemorrhagic stroke.[18]

Anticoagulation

Warfarin prevents stroke in atrial fibrillation and appears safe even in the very elderly. Newer oral anticoagulant drugs (dabigatran, rivaroxaban and apixaban) offer an alternative to warfarin, with predictable anticoagulation from a fixed dose, no requirement for international normalized ratio monitoring, reduced bleeding risk and/or reduced stroke risk[19]: disadvantages include lack of laboratory tests for anticoagulant effect, lack of a reliable means of reversing anticoagulation, and need for renal function checks.

Carotid endarterectomy

Surgical removal of atherosclerotic material from the carotid arteries prevents ipsilateral stroke in recently symptomatic carotid stenosis. Benefit is greatest within 2 weeks of symptoms and declines rapidly thereafter, with no benefit after 3 months.[20] Early surgery is beneficial with stenosis of 50% or greater, later surgery if 70% or greater. Stenting carries a higher short-term risk, especially in people aged 70 years or older, but may be an alternative in younger patients.[21] ◆

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