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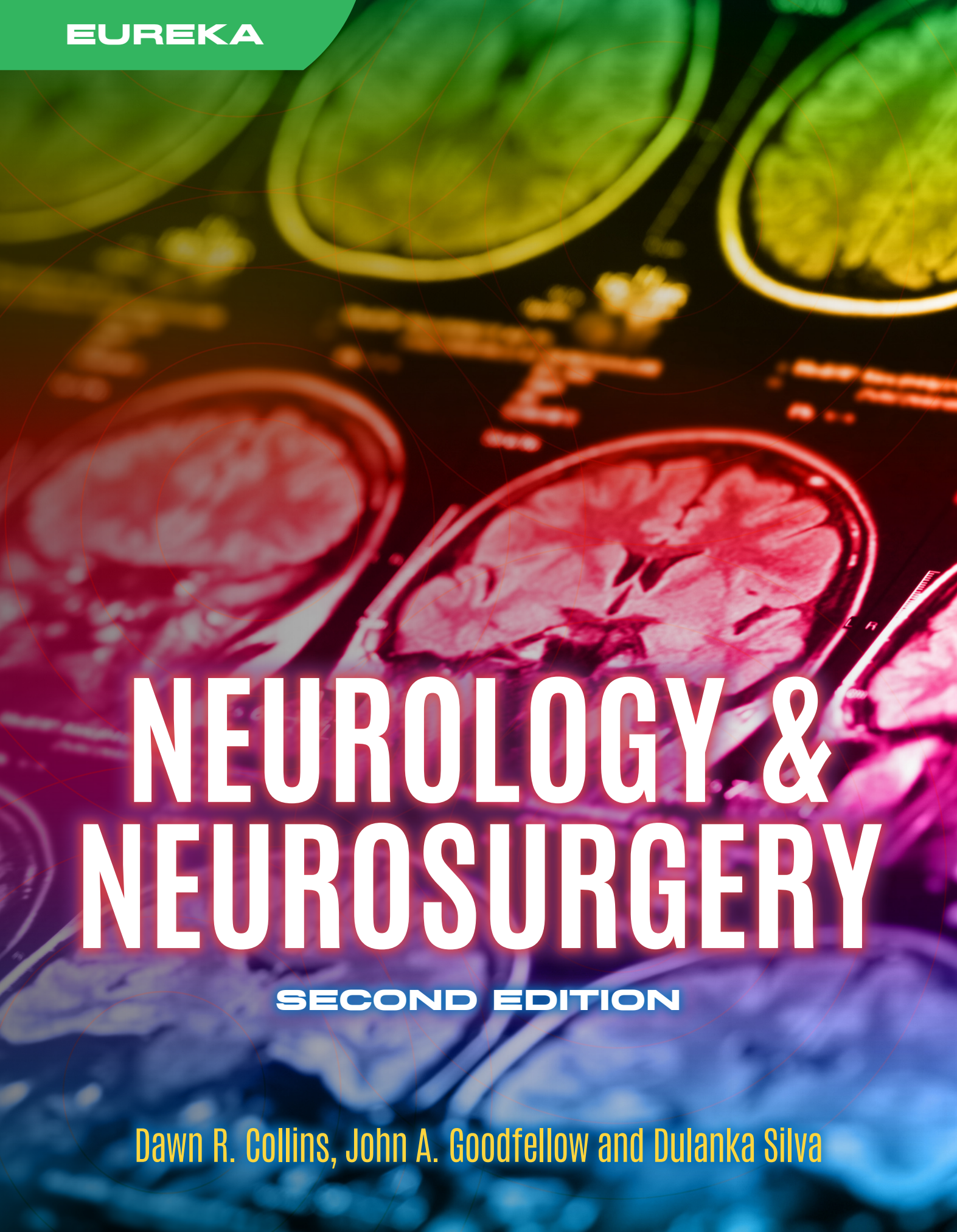

NEUROLOGY & NEUROSURGERY

SECOND EDITION

Dawn R. Collins, John A. Goodfellow and Dulanka Silva

NEUROLOGY & NEUROSURGERY

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Contents

Preface to the second edition

Neurology and neurosurgery inspire a mixture of fear and fascination in most medical students due to the perceived complexity of the nervous system. *Eureka Neurology & Neurosurgery*, second edition demystifies the nervous system, and the diagnosis and management of neurological disorders, by integrating the core neuroscience and clinical knowledge in an accessible way.

Chapter 1 covers core neuroscience: the structural framework that underpins clinical practice. *Chapter 2* lays out the tools required to apply this knowledge when evaluating and managing neurological patients. Subsequent chapters describe the spectrum of neurological and neurosurgical disorders, from infections to traumatic injury. Clinical cases are brought to life using graphic narratives and neuroradiological imaging, while figures and boxes simplify key concepts and provide clinical correlates. Dedicated chapters cover emergency presentations and the integrated management of patients with chronic neurological conditions.

Chapter 7 has been updated for this second edition to encompass the substantial progress that has been made in classification of brain tumours with reference to the importance of now not only grading and diagnosing with histopathology, but molecular phenotyping in order to subclassify brain tumours.

We hope you enjoy this book and that it provides you with confidence when approaching patients with neurological disorders.

Dawn Collins
John Goodfellow
Dulanka Silva

Self-assessment is an important part of study for any medical specialty. Clinical single best answer (SBA) questions on neurology and neurosurgery are a useful revision aid, so we have produced a broad range of these, along with detailed answers. They can be found on the Resources tab on the page for this book at www.scionpublishing.com/eureka-neurology.

About the authors

Dawn Collins is Associate Professor in Neurobiology at Warwick Medical School. She has been teaching neurobiology and neuropharmacology to the graduate-entry medical students and undergraduate students for over 20 years, and currently leads teaching on neurobiology and case-based learning for the undergraduate Health and Medical Sciences course.

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Abbreviations

ABCDE	Airway, Breathing, Circulation, Disability, Exposure
ACE	angiotensin-converting enzyme
ADC	apparent diffusion coefficient
AIDS	acquired immunodeficiency syndrome
AMA	antimitochondrial antibody
AMPLE	Allergies, Medications, Past medical history, Last meal, Events surrounding injury
ANA	antinuclear autoantibody
ANCA	antineutrophil cytoplasmic antibody
anti-dsDNA	anti-double-stranded DNA autoantibody
ATLS	Advanced Trauma Life Support
AVM	arteriovenous malformation
AZT	azidothymidine
BOLD	blood oxygenation level-dependent
BP	blood pressure
CJD	Creutzfeldt–Jakob disease
CN	cranial nerve
CRP	C-reactive protein
CSF	cerebrospinal fluid
CT	computed tomography
DMPK	dystrophia myotonica protein kinase
DWI	diffusion-weighted imaging
EEG	electroencephalogram or encephalography
ESR	erythrocyte sedimentation rate
FLAIR	fluid-attenuated inversion recovery
GCS	Glasgow Coma Scale
HAART	highly active antiretroviral therapy
HIV	human immunodeficiency virus
ICHD	International Classification of Headache Disorders
ICP	intracranial pressure
LMN	lower motor neurone
MND	motor neurone disease
MPTP	1-methyl-4-phenyl-1,2,3,6- tetrahydropyridine
MR	magnetic resonance
MRI	magnetic resonance imaging
MS	multiple sclerosis
NMJ	neuromuscular junction
NMDA	*N*-methyl-D-aspartate
NSAID	non-steroidal anti-inflammatory drug
OCB	oligoclonal band
PCR	polymerase chain reaction
PET	positron emission tomography
PNS	parasympathetic nervous system
SLE	systemic lupus erythematosus
SNS	sympathetic nervous system
SPECT	single-photon emission computed tomography
STIR	short tau inversion recovery
SUDEP	sudden unexpected death in epilepsy
SUNCT	short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing
TIA	transient ischaemic attack
UMN	upper motor neurone
V	volume
$\mathbf{V_{blood}}$	volume of blood
$\mathbf{V_{brain}}$	volume of brain
$\mathbf{V_{cerebrospinal\ fluid}}$	volume of cerebrospinal fluid
$\mathbf{V_{extra\ mass}}$	volume of extra mass
$\mathbf{V_{total}}$	total intracranial volume
WHO	World Health Organization

Chapter 6
Neurovascular disease

Starter questions

1. **Do people have 'silent strokes'?**
2. **Why does a stroke need rapid treatment?**
3. **Why is it important to treat transient ischaemic attacks?**
4. **Can rehabilitation reverse brain tissue damage?**

Answers to questions are to be found in *Section 6.8*.

6.1 Introduction

The term neurovascular disease encompasses all disorders affecting the vessels of the central nervous system. Neurovascular diseases arise as a result of:

- pathological changes affecting the vessels, e.g. acute and chronic occlusions of arteries or veins leading to ischaemia and ultimately, if blood flow does not normalise, infarction (death of brain tissue), or
- acquired or congenital structural abnormalities that increase the likelihood of vessels haemorrhaging intracranially or causing mass (or pressure) effect, e.g. arteriovenous malformations (AVM) (which can cause any of these effects).

Stroke is the rapid onset of focal neurological deficits corresponding to dysfunction in specific vascular territories of the brain. It is the most common manifestation of neurovascular disease. Most strokes are due to cerebral ischaemia and infarction, almost always arterial rather than venous, but about a fifth are the result of intracranial arterial haemorrhage.

Stroke is the third most common cause of death after cardiac disease and cancer, and the commonest cause of neurological disability. Outcomes are greatly improved by immediate recognition and transfer for early treatment. Therefore the ability to recognise the more common presentations of stroke is essential for all doctors. 'Cerebrovascular' disease refers to vascular diseases affecting the cerebrum or cerebral hemispheres, but is used interchangeably with 'neurovascular' in practice.

Case 6.1 Blackout

Presentation

James Lau, a 38-year-old accountant, presents to the emergency department having collapsed at work.

Initial interpretation

Neurological and cardiac pathologies are very high on the list of causes of collapse (**Table 6.1**). The acute nature of James's symptoms suggests a vascular insult to the brain or heart.

History

James is drowsy and unable to provide a history. However, a colleague witnessed the event. James complained to him of a severe headache after going to the bathroom. He had described it as the worst headache of his life. He complained of neck stiffness and of light hurting his eyes.

Case 6.1 *continued*

Interpretation of history

There are no features, such as chest pain or shortness of breath, to suggest a cardiac cause. The presentation is very typical for acute subarachnoid haemorrhage: rapid speed of onset, 'worst headache ever' description and meningism (neck stiffness and photophobia).

Further history

An hour later, James collapsed and was unresponsive for a few minutes. However, he recovered slowly afterwards. His colleagues say he did not have a seizure. An ambulance brought him to hospital. He has no medical or family history but is a heavy smoker.

Examination

After initial Advanced Life Support resuscitation and stabilisation, James's neurological status is assessed. He opens his eyes to voice (eye response, E3), is confused (verbal response, V4) and obeys commands (motor response, M6), giving a total GCS score of 13/15. He has weakness down his left side, his pupils are equal and respond to light, and he has meningism with neck stiffness.

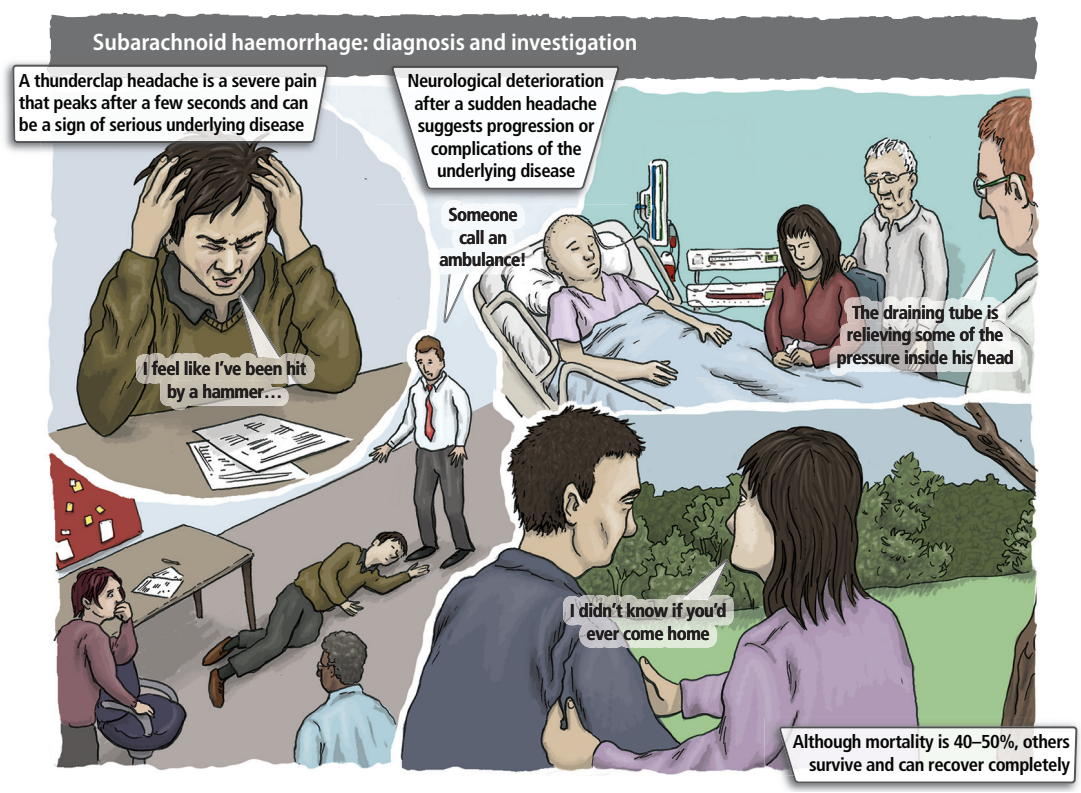
Interpretation of findings

The initial clinical history is consistent with aneurysmal subarachnoid haemorrhage. James's GCS score was 15 at first, but his subsequent collapse an hour later suggests possible complications after subarachnoid haemorrhage. The priorities are to:

- confirm the subarachnoid haemorrhage with computed tomography (CT) of the brain
- investigate for an underlying vascular lesion, predominantly a cerebral aneurysm and less commonly an arteriovenous malformation.

Table 6.1 *Common causes of sudden-onset collapse*

System	Cause
Nervous system	Acute intracranial haemorrhage: subarachnoid, intracerebral (spontaneous or caused by an underlying lesion) or intraventricular
	Acute ischaemic stroke
	Seizure
	Acute hydrocephalus
Cardiac system	Acute myocardial infarction
	Acute arrhythmia
	Aortic dissection
	Cardiac arrest
Miscellaneous	Pulmonary embolism



Case 6.1 *continued*

Investigations

An urgent brain CT scan confirms diffuse subarachnoid haemorrhage (**Figure 6.1**). There is blood in the ventricles (intraventricular haemorrhage), which increases the risk of hydrocephalus. On the unenhanced scan is a blister, which suggests a right middle cerebral artery aneurysm as the cause.

Diagnosis

James initially had a ruptured middle cerebral artery aneurysm with subarachnoid haemorrhage. The subsequent collapse was probably a consequence of acute complications of aneurysmal subarachnoid haemorrhage:

- rerupture and rebleeding
- acute hydrocephalus (likely in this case because of the intraventricular haemorrhage, which occludes cerebrospinal fluid pathways)
- seizures.

Complications such as vasospasm (see *Section 6.4*) and electrolyte abnormalities, especially hyponatraemia, usually occur a few days later.

James is urgently referred to neurosurgery. CT angiography confirms the aneurysm location. Medical management measures for acute subarachnoid haemorrhage are initiated (**Table 6.2**), and he undergoes a cerebrospinal fluid diversion procedure to relieve the hydrocephalus. He subsequently undergoes interventional neuroradiological coil embolisation of the aneurysm.

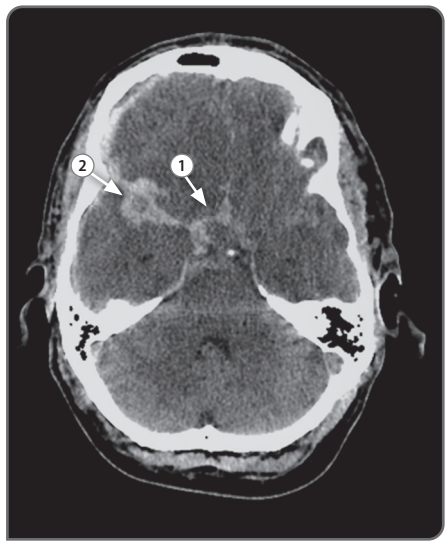


Figure 6.1 Axial CT, without contrast, at the level of the basal cisterns. Extensive subarachnoid haemorrhage is visible near the circle of Willis (1). The blister in the right Sylvian fissure suggests a middle cerebral artery aneurysm (2).

Table 6.2 ***Acute subarachnoid haemorrhage: medical management measures instituted as soon as haemorrhage has been diagnosed***

Therapy	Rationale
Nimodipine (60 mg every 4 h for 21 days)	Reduces risk of cerebral vessel vasoconstriction and consequent ischaemia and infarction (risk is increased after aneurysmal subarachnoid haemorrhage)
Adequate hydration (3 L/24 h with intravenous normal, 0.9%, saline)	Prevents dehydration and consequent reduced cerebral perfusion, which increases risk of ischaemia and infarction
Monitoring and regulation of blood pressure	Acutely the body autoregulates blood pressure, so optimal blood pressure targets are uncertain Excessive reduction in blood pressure can precipitate ischaemia and infarction due to impaired blood flow Excessive increased blood pressure before the aneurysm has been treated risks repeat rupture and rebleeding A balance between these two extremes is required
Monitoring and treatment of complications	Reduce risk of and treat: ■ rebleeding ■ vasospasm ■ hydrocephalus ■ seizures ■ electrolyte (especially sodium) abnormalities (e.g. hyponatraemia) ■ cardiac complications (e.g. neurogenic pulmonary oedema and myocardial infarction)

Case 6.2 Sudden-onset weakness

Presentation

Sheila Patterson, aged 68 years, suddenly develops right-sided face, arm and leg weakness and numbness while out shopping. The acute stroke team assess her and confirm the time of onset as 45 min ago.

Initial interpretation

Sudden-onset unilateral weakness and numbness represent disruption of motor and sensory function in the left hemisphere, for which the most likely cause is an acute stroke. Further assessment is needed to identify which other brain regions are affected, and thereby classify the stroke syndrome and determine suitability for thrombolysis ('clot busting') to reopen the blocked artery.

History

Mrs Patterson has hypertension, for which she takes an angiotensin-converting enzyme inhibitor. She was otherwise well and fully independent before the event. She cannot feel her right side and denies other neurological symptoms. Her daughter, who is with her, confirms this.

Interpretation of history

Time of onset is clear from a witnessed history. Right-sided weakness and numbness without other symptoms could be from a lacunar stroke, damaging internal capsule fibres carrying motor and sensory pathways to and from the cortex, or partial anterior circulation stroke, damaging a wider area including the sensory and motor cortices. Hypertension is a risk factor for stroke, and there are no contraindications for thrombolysis in the history.

Further history

Mrs Patterson denies a hemianopia, language disturbance, diplopia, vertigo and headache. The absence of these other symptoms makes partial or total anterior circulation stroke unlikely. She has had no recent surgery, rectal bleeding, haemoptysis, haematemesis or chest pain, which would have suggested occult gastrointestinal or pulmonary haemorrhage, or aortic dissection; these conditions are contraindications to thrombolysis.

Examination

Mrs Patterson has right-sided flaccid paralysis of her face, arm and leg. Her GCS score is 15/15, and cranial nerve function is normal. She has no visual field defect, neglect or language disturbance. There are brisk reflexes and up-going (extensor) plantar on the right. Blood pressure is 175/98 mmHg, with normal sinus rhythm on electrocardiogram.

Interpretation of findings

A clinical diagnosis of a left (side of brain lesion) lacunar stroke can be made: right-sided weakness and sensory loss of rapid onset, and absence of signs indicating involvement of other cortical or brainstem regions. This localises the stroke to the left internal capsule or basal ganglia. Hypertension is the only risk factor identified. She has no contraindications to thrombolysis (see **Table 6.7**). Her stroke is significantly disabling. She requires an immediate brain CT scan to exclude an intracerebral haemorrhage before thrombolysis.

Investigation

CT reveals a left basal ganglia haemorrhage (**Figure 6.2**). No other imaging is required, because the location of the haemorrhage in the presence of appropriate risk factors is typical for hypertension. When the location is atypical for hypertension, a CT angiogram may be done to exclude an underlying vascular malformation, or a delayed MRI (e.g. a few months later) to exclude an underlying tumour.

Diagnosis

Thrombolysis is not given to Mrs Patterson, because this would worsen the underlying pathological process of haemorrhage. Her blood pressure is closely monitored during the acute phase to avoid dangerous extremes: if too high, extension of haemorrhage usually occurs; if too low, underperfusion of vulnerable tissue with subsequent infarction. She receives intensive inpatient physiotherapy, speech therapy and occupational therapy to improve her functional recovery. She is then discharged on an additional antihypertensive agent and a statin for secondary prevention.

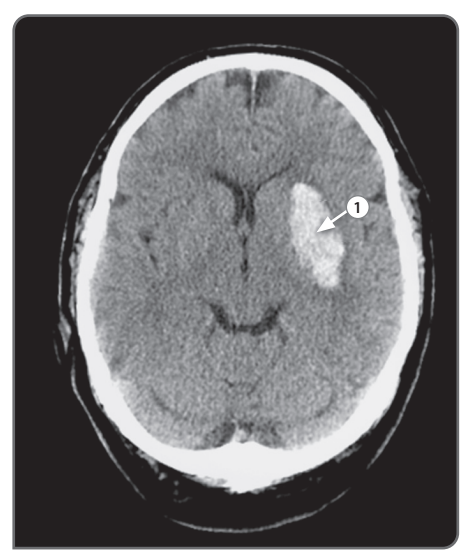


Figure 6.2 Acute hyperdense clot (1) confirming left acute basal ganglia haemorrhagic stroke, probably related to hypertension.

6.2 Ischaemic and haemorrhagic stroke

Stroke describes the sudden (seconds to minutes) onset of focal symptoms or signs of brain dysfunction arising from ischaemia, infarction or haemorrhage localised to a specific vascular territory. The neurological deficits persist for ≥24 h.

Stroke symptoms or signs that resolve completely within 24 h represent a transient ischaemic attack (TIA), which is discussed in detail in *Section 6.3*. The early risk of stroke after TIA is high (7-day risk, 8–12%; 30-day risk, 18%).

The annual incidence of stroke is 240 in 100,000 in the UK.

Aetiology and pathogenesis

About 80% of strokes are ischaemic and usually caused by near-complete occlusion of a cerebral vessel. The obstruction impairs the delivery of oxygen and nutrients to brain tissue, thereby causing tissue damage and neurological dysfunction. If vascular supply is not restored, infarction ('death') of brain tissue ensues.

The remaining 20% of strokes are haemorrhagic. In haemorrhagic stroke, blood vessels rupture, resulting in acute bleeding into brain substance.

Table 6.3 summarises risk factors for strokes. Identifying and targeting these for therapy remains the cornerstone of stroke management.

Ischaemic stroke

Vascular occlusion most often occurs because of thromboembolism: thrombosis (formation of a blood clot, 'thrombus') and embolisation (fragments of the blood clot travelling downstream).

Three factors precipitate thrombosis (Virchow's triad). They are:

- stasis of blood
- vessel wall changes (i.e. injury to endothelium)
- changes in blood constituency (e.g. blood hypercoagulability, an abnormal increase in blood-clotting tendency).

Any pathological process increasing these factors can lead to vascular thrombosis.

Table 6.3 *Major risk factors for acute ischaemic stroke*

Risk factor	Relative risk of developing stroke
Hypertension 160/95 mmHg compared with 120/80 mmHg	7
Age >75 years compared with 55–64 years	5
Atrial fibrillation	5
Previous transient ischaemic attack or stroke	5
Ischaemic heart disease	3
Diabetes	2
Smoking	2

Atherosclerosis

The commonest cause of arterial thromboembolism is atherosclerosis, a progressive inflammatory thickening of arterial walls. Atherosclerosis begins with endothelial injury, which leads to growing 'plaques' of white blood cells, fat deposits and eventual calcification. It occurs with normal ageing but is increased by smoking, hypertension, diabetes and excessive blood cholesterol.

The atherosclerotic plaque increasingly occludes the artery as it grows. It can become unstable and rupture, leading to acute clot (thrombi) formation that completely occlude the artery (thrombosis). Alternatively, a fragment (an embolus) may break off and occlude a vessel downstream of the plaque (**Figure 6.3**).

Cardioembolism

Acute clots may also form in the heart because of changes in blood flow, for example in patients with arrhythmias (such as atrial fibrillation), valvular heart disease, prosthetic heart valves and congenital defects, or after myocardial infarction. These clots may embolise to cerebral arteries, thereby causing an ischaemic stroke (cardioembolism).

Embolism

Most ischaemic strokes result from clots originating from atherosclerotic plaques (atherothromboembolism) or the heart (cardioembolism). However, rarely, other substances can embolise to the brain. These include tumour, septic (infective), air and fat emboli.

Other conditions

Various conditions increase the likelihood of ischaemic stroke, including:

- inflammatory vascular diseases (e.g. vasculitic syndromes such as polyarteritis nodosa and granulomatosis with polyangiitis, previously called Wegener's granulomatosis)

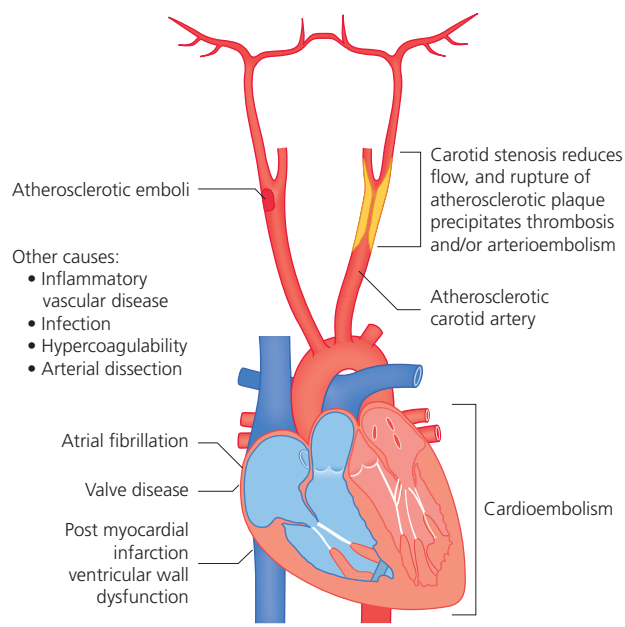


Figure 6.3 Causes of ischaemic stroke.

- collagen vascular diseases (e.g. rheumatoid arthritis and Marfan's syndrome)
- infection (e.g. syphilis, HIV, meningitis and tuberculosis)
- arterial dissection (rupture in the vessel wall occurring spontaneously or because of trauma or predisposed weakness)
- blood diseases predisposing to excessive clotting (thrombophilias and polycythaemia).

Haemorrhagic stroke

Most haemorrhagic strokes are intracerebral (75%); the remaining 25% are subarachnoid. Haemorrhage precipitates:

- loss of cerebrovascular autoregulation
- disruption of the blood–brain barrier
- cerebral oedema (cytotoxic and vasogenic)
- neuronal damage caused by the toxicity of blood products and mass effect of an acute blood clot
- increase in intracranial pressure
- hydrocephalus if the haemorrhage ruptures into the ventricular system.

The most common cause of spontaneous subarachnoid haemorrhage is rupture of an intracranial aneurysm.

Intracerebral haemorrhage

The commonest cause of spontaneous intracerebral haemorrhage is rupture of small cerebral vessels (perforating arteries) with walls weakened by hypertension. Other causes include:

- arteriovenous malformations (AVM; see *Section 6.5*)
- amyloid angiopathy (degenerative blood vessel weakening as a result of amyloid deposition)
- aneurysm (see *Section 6.4*) rupture
- tumours (haemorrhage in an intracranial tumour is sometimes its initial presentation)
- clotting dysfunction (e.g. from the use of anticoagulant or antiplatelet drugs, or after thrombolytic therapy for ischaemic stroke)
- haemorrhage secondary to intracranial vein thrombosis.

Clinical features

History and examination are crucial to confirm signs and symptoms, identify risk factors and broadly localise the lesion. Acute stroke services are contacted in all cases of suspected stroke to arrange urgent assessment, investigation and management.

The hallmark of stroke, as with most neurovascular pathologies, is the sudden and rapid onset of neurological dysfunction.

Oxford classification of stroke

The Oxford classification divides stroke into four categories correlating the clinical features arising from dysfunction in brain regions with the main blood vessels affected (**Table 6.4**). It is the most commonly used classification in the clinical assessment of acute stroke patients, because it is easy and quick to do, and the results are highly reproducible.

Table 6.4 ***The Oxford classification system for stroke***

Syndrome	Features
Total anterior circulation syndrome (TACS)	All of: ■ motor or sensory deficit* (usually contralateral) ■ hemianopia (visual field deficit – usually contralateral homonymous hemianopia) ■ higher cortical dysfunction†
Partial anterior circulation syndrome (PACS)	Two of: ■ motor or sensory deficit* ■ hemianopia ■ higher cortical dysfunction†
Lacunar syndrome	One of: ■ pure motor deficit* (lesion usually in posterior limb of internal capsule) ■ pure sensory deficit* (lesion usually in thalamus) ■ sensory and motor deficit* ■ ataxic hemiparesis (ataxia and hemiparesis affecting the same side; lesion usually in ventral pons with pontocerebellar fibre disruption) Without either: ■ higher cortical dysfunction† ■ posterior circulation syndrome symptoms
Posterior circulation syndrome (POCS)	Any of: ■ isolated hemianopia (lesion in occipital lobe) ■ bilateral motor and sensory deficit ■ brainstem signs and symptoms ■ cranial nerve deficits (e.g. diplopia, facial sensory loss, lower motor neurone facial nerve palsy, vertigo, hearing loss, dysphagia and dysarthria) ■ cerebellar signs and symptoms (e.g. ataxia, nystagmus, past pointing, intention tremor, dysarthria and slurred speech)

*Affecting the face, arm or leg (independently or in combination)

†Higher cortical dysfunction gives rise to various deficits that depend on whether the dominant or non-dominant hemisphere is affected.

Anterior circulation syndromes

These syndromes affect brain regions supplied by the internal carotid arteries and its major terminal branches, i.e. the anterior cerebral and middle cerebral arteries.

Posterior circulation syndromes

These affect brain regions supplied by the vertebrobasilar vessels and their associated branches: the vertebral, basilar, posterior inferior cerebellar, anterior inferior cerebellar, superior cerebellar and posterior cerebral arteries.

Posterior circulation syndromes can present with a bewildering range of clinical findings. This variety is a consequence of brainstem involvement; many motor, sensory and cranial nuclei and nerve tracts can be affected.

Lacunar syndromes

These syndromes affect brain regions supplied by deep penetrating perforator arteries from either the anterior or posterior circulation. These arteries supply deep white matter, for example the internal capsule, or deep subcortical structures, such as the thalamus and basal ganglia. 'Lacunar' derives from 'lacunae', the small CSF-filled spaces in the deep grey matter.

Hemispheric dominance

The clinical pattern of higher cortical deficits also indicates whether the hemisphere involved is dominant or non-dominant (see *Section 1.5.3*).

With involvement of the dominant hemisphere (usually the left):

- the patient has insight
- they may also have aphasia and difficulty reading, writing and calculating.

If the non-dominant hemisphere (usually the right) is involved:

- the patient lacks insight
- they may have neglect, spatial disorientation and apraxias (e.g. difficulty dressing and constructional apraxia).

Specific vascular territories

The Oxford classification localises the lesion to a broad vascular territory. However, more specific syndromes from dysfunction of specific vessels usually present with stereotypical deficits (see **Table 6.5**).

Distinguishing between ischaemic and haemorrhagic stroke

It is difficult to differentiate between ischaemic and haemorrhagic stroke on the basis of clinical assessment alone. For example, headache is more common with haemorrhage than with ischaemia. Neuroimaging is the definitive way to distinguish between the two.

Some haemorrhagic strokes have a characteristic constellation of symptoms. For example, some posterior communicating artery aneurysms compress cranial nerve III to produce a third nerve palsy. Its clinical features are ptosis, restriction of the movement of eye muscles innervated by the nerve, pain in the eye (or head) and a dilated pupil from compression of the nerve's parasympathetic fibres.

Diagnostic approach

The principles of stroke assessment are shown in **Figure 6.4**. Early referral to acute stroke services is crucial for assessment, evaluation of suitability for thrombolysis, investigation and coordinating management.

Differential diagnoses for stroke include:

- hypoglycaemia and hyperglycaemia
- complicated migraine (with prominence of atypical features for stroke: migraine history, positive visual phenomena and paraesthesia)
- sepsis (especially in the elderly)
- seizures
- metabolic abnormalities (e.g. electrolyte disturbances and hepatic encephalopathy)
- drug overdose or effects of toxins

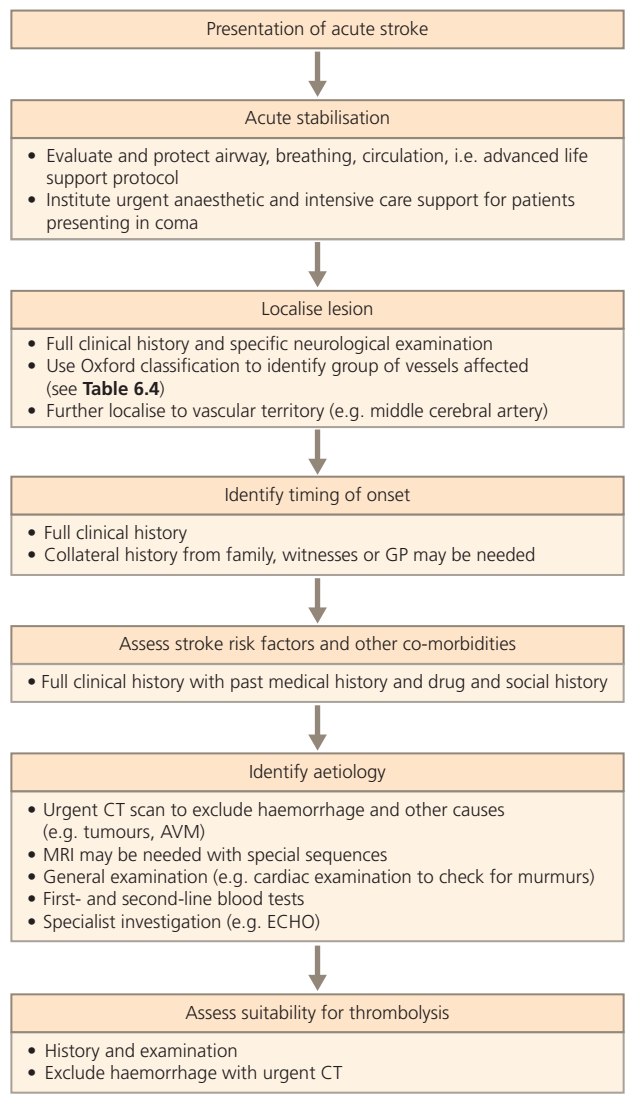


Figure 6.4 Diagnostic approach for a patient presenting with acute stroke. Identification of the cause may have to be delayed until after acute management. If thrombolysis is being considered, it is critical to exclude haemorrhage by urgent imaging.

Table 6.5 ***Typical symptoms and signs associated with specific stroke syndromes***

Affected vessel	Classic clinical features
Anterior cerebral artery	Contralateral lower limb motor and sensory deficit Urinary or bladder sphincter disturbance (e.g. incontinence) Behavioural change and disinhibition
Middle cerebral artery	Contralateral motor deficit (face and upper limb affected mainly, with relative sparing of lower limb) Contralateral sensory deficit Higher cortical dysfunction Contralateral hemianopia
Vertebral artery*	Occlusion of one side is usually compensated by anastomoses If the other vertebral artery is hypoplastic (congenitally narrow), occlusion is similar to basilar artery occlusion
Basilar artery†	Total basilar occlusion: ■ coma (midbrain damage) ■ bilateral motor and sensory dysfunction (major tracts) ■ cerebellar signs ■ cranial nerve signs ■ top of basilar occlusion is similar to posterior cerebral artery occlusion
Posterior inferior cerebellar artery	Contralateral: ■ loss of pain and temperature sensation in body (spinothalamic tract) Ipsilateral: ■ loss of pain and temperature in face (CN V) ■ vertigo (CN VIII) ■ nystagmus and ataxia (cerebellar tracts) ■ dysphagia and dysarthria (CN IX and CN X) ■ Horner's syndrome (sympathetic chain)
Posterior cerebral artery	Cortical occlusion: ■ contralateral homonymous hemianopia (occipital lobe) ■ memory disturbance (temporal lobe) Thalamic damage: ■ chorea or hemiballismus movements with contralateral hemisensory loss Midbrain damage: ■ gaze palsies ■ pupillary abnormalities ■ reduced consciousness level

CN, cranial nerve.

*The posterior inferior cerebellar artery is usually a branch of the vertebral artery.

†The anterior inferior cerebellar, superior cerebellar and posterior cerebral arteries are branches of the basilar artery; many perforators also originate from the basilar artery and supply the brainstem.

- other intracranial lesions (e.g. abscess, tumour, acute hydrocephalus and pneumocephalus).

Investigations

Urgent CT is used to differentiate ischaemic and haemorrhagic stroke. It is also used to identify other intracranial pathology. Acute management is then started.

Most infarcts are caused by emboli from arterial or cardiac thrombi (atherothromboembolism or cardioembolism, respectively) in a patient with significant cardiovascular risk factors such as hypertension, smoking and diabetes. Younger patients may have a rare cause of their infarct, necessitating extensive investigation after acute management.

Imaging in ischaemic stroke

The CT scan can be normal in the first few hours after an ischaemic stroke, especially in cases of posterior circulation syndromes. It can take up to 24 h for infarction to become well established on CT (**Figure 6.5**). Early subtle features of stroke to identify in an initially normal-looking CT are:

- sulcal effacement (the cortical sulci lose definition because of subtle oedema)
- loss of grey-white differentiation (oedema causes subtle loss of this distinction, especially in the basal ganglia and insular cortex)
- dense middle cerebral artery (an occluded middle cerebral artery appears hyperdense on CT).

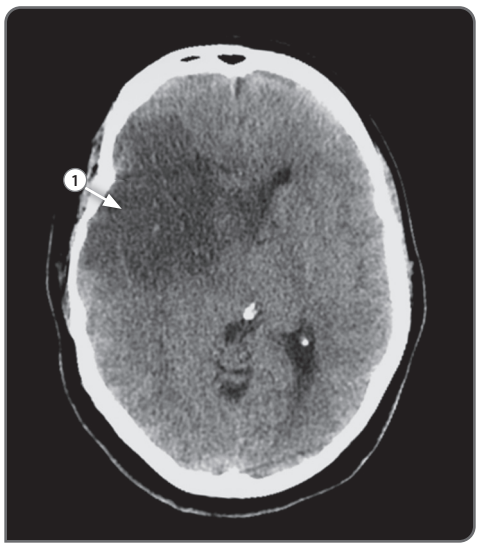


Figure 6.5 Axial non-contrast CT 24 h after symptom onset. The initial scan was normal. However, this scan shows an established right middle cerebral artery infarct (1) with an extensive area of hypodensity.

MRI is more sensitive; it may confirm acute ischaemia in a patient whose CT scan is normal. Special sequences, such as diffusion-weighted imaging, show acute ischaemia in its earliest stages (**Figure 6.6**).

Further imaging includes:

- carotid imaging (ultrasound, CT or magnetic resonance angiography) to assess for atherosclerotic narrowing of carotid arteries
- cardiac echocardiography to assess for valvular heart disease, congenital defects and possible thrombi or embolic sources in the presence of arrhythmias
- digital subtraction cerebral angiography to assess cerebral vascular stenosis.

Imaging in haemorrhagic stroke

CT rapidly localises the haemorrhage. It also visualises associated complications such as intraventricular extension of haemorrhage and mass effect.

If aneurysm or AVM is suspected, CT angiography, magnetic resonance angiography or digital subtraction cerebral angiography is essential. Haemorrhagic transformation (when an area of ischaemic brain becomes fragile and bleeds) can also occur after acute thrombosis, for example in sinuses or cortical veins.

An MRI scan is often done 6–8 weeks after treatment of haemorrhagic stroke, especially in younger patients. This is because acute haemorrhage may initially hide and thus prevent detection of an underlying tumour or vascular lesion such as aneurysm and AVM.

Electrocardiography

This is used to identify cardiac arrhythmias as either a mimic of stroke, such as heart block leading to collapse, or a cause, for example atrial fibrillation precipitating embolic stroke.

Blood tests

Hypoglycaemia can cause rapid onset focal neurological deficits. Therefore serum glucose concentration is always measured.

Other tests depend on the suspected cause.

- First-line tests (e.g. measurement of glucose, cholesterol and electrolytes) are carried out to guide acute management and ascertain risk factors
- Second-line tests (e.g. thrombophilia screen, blood cultures and vasculitic screen) are done to assess the rare causes of strokes.

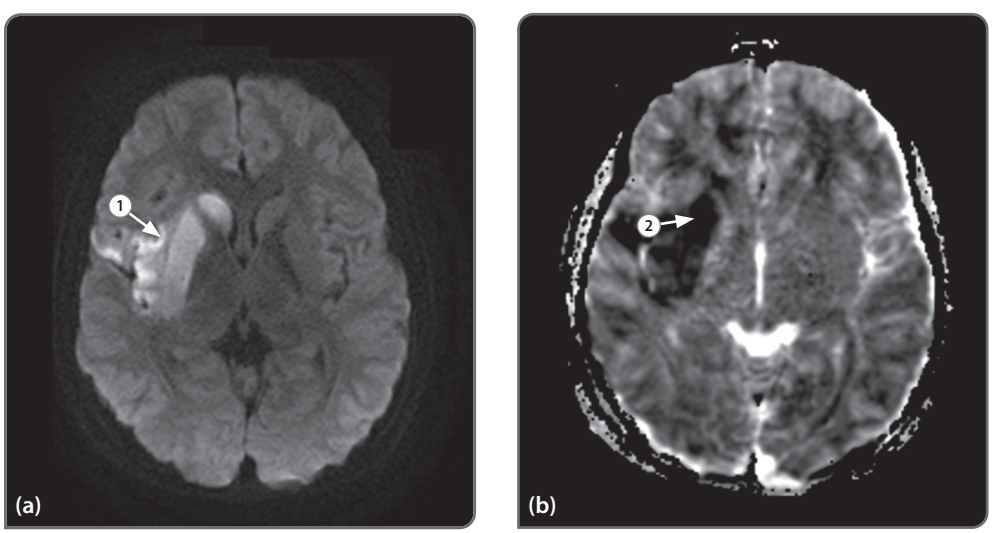


Figure 6.6 Axial MRI: (a) diffusion-weighted imaging (DWI) and (b) apparent diffusion coefficient (ADC) sequences from the same patient. These were obtained immediately after normal CT and in the early stages show restricted diffusion: high bright signal on DWI (1) and low dark signal on ADC (2) in the right middle cerebral artery territory. Signs of ischaemia and infarction can be detected on DWI much earlier than on CT.

Management

Acute stroke management is divided into general principles (**Table 6.6**) and specific interventions.

Treatment is conservative in most patients with spontaneous haemorrhagic stroke not caused by aneurysm or AVM.

Medication

Medical management of stroke utilises a combination of pharmacological agents to limit the severity of ischaemic injury and mainly secondary prevention with control of risk factors.

Acute ischaemic stroke

The aim is to salvage the 'ischaemic penumbra' and limit the spread of infarction. The penumbra is the tissue surrounding the infarcted regions that has reduced blood flow and is still functional.

Thrombolysis Also called 'clot busting', thrombolysis is beneficial in patients with a major stroke and a large ischaemic penumbra. Intravenous recombinant tissue plasminogen activator (alteplase) is given within 3.5 h of onset of stroke symptoms to reperfuse ischaemic tissue. The benefit is less disability at 3 months rather than acute symptom reversal; the earlier it is given, i.e. within 90 minutes, the better the outcome.

The major complication of thrombolysis is precipitation of acute haemorrhage in an ischaemic or infarcted region.

Thrombolysis should only be undertaken in specialised centres because of the number of contraindications (**Table 6.7**) and the potential severity of adverse events.

Antiplatelet agents These inhibit platelet activity. Unless imaging shows primary haemorrhage, antiplatelet agents are initiated after acute ischaemic stroke. Aspirin within 48 h acts as secondary prevention; it reduces mortality and recurrent stroke. It is given for 2 weeks, and then clopidogrel, another antiplatelet, is given lifelong.

Anticoagulant agents These inhibit the clotting cascade. Antiplatelet agents are replaced after 2 weeks with warfarin anticoagulation in patients with chronic non-valvular non-rheumatic atrial fibrillation or a cardioembolic cause such as prosthetic heart valve. It is superior to antiplatelet agents in reducing ischaemic stroke risk in these patients; thus it provides both primary and secondary prevention. Anticoagulation does more harm than good in other causes of ischaemic stroke.

Table 6.6 ***General principles in the management of acute stroke***

Principle	Aim(s)	Management method(s)
Treatment location	To improve survival (management in dedicated stroke units reduces mortality by 30%)	Admission to stroke unit or intensive care unit
Airway	To avoid hypoxia or aspiration and maintain a patent airway	Airway measures and anaesthetic support in cases of coma
BP control	Optimal management uncertain, because the brain may attempt to autoregulate Treatment of even high levels of BP may harm by compromising cerebral perfusion	Treat if complications of hypertension (e.g. hypertensive encephalopathy, aortic dissection and cardiac failure) are present If sustained, treat BP >220/120 mmHg in ischaemic and BP >185/115 mmHg in haemorrhagic stroke
Glucose control	In acute stroke, avoid hyperglycaemia, which is associated with poor outcome	Aim for normal levels
Hydration and nutritional support	To prevent dehydration To ensure good nutritional support	Intravenous fluids Nasogastric feeding if patient dysphagic
Deep vein thrombosis prophylaxis	Prevention of deep vein thromboses and associated pulmonary embolism as a result of immobility following stroke	Timing of initiation of prophylactic clexane following stroke is commonly debated. Most will start clexane 48–72 h following acute ischaemic stroke. Timing of clexane initiation following haemorrhagic stroke is more controversial Intermittent use of pneumatic compression stockings as mechanical prophylaxis
Seizures	To reduce risk of focal or generalised seizure (which occur in about 2% of patients)	Antiepileptic drugs as required
Physiotherapy	To prevent contractures To restore function To prevent pressure sores	Early mobilisation Early rehabilitation referral Strategies to cope with impairment
Neuropsychiatric complications	To prevent depression	Antidepressants
Communication	To ensure good communication with patients and family members	Set realistic goals

BP, blood pressure.

These principles apply to all types of ischaemic and haemorrhagic stroke, except aneurysmal subarachnoid haemorrhage.

Table 6.7 *Contraindications to thrombolysis*

Clinical feature	Contraindications
Presentation	Onset unclear or >3.5 h ago
	Seizure since onset
	Invasive or surgical procedure in previous 3 weeks
	Cardiopulmonary resuscitation
	Pregnancy or recent obstetric delivery
	Minor symptoms or improving
	Significant premorbid dependence
Bleeding disorder	Previous intracranial haemorrhage
	Active bleeding
	Active peptic ulcer or gastrointestinal bleeding
	Current anticoagulation use or $<100 \times 10^9$ platelets/L
	Severe liver disease or varices, or portal hypertension
Cranial disorder	Stroke in preceding 3 months
	Structural cerebrovascular disease (e.g. aneurysm or AVM)
	Major infarct or haemorrhage on CT
Cardiac disorder	Aortic dissection
	Severe hypertension (blood pressure >220/130 mmHg)

Acute haemorrhagic stroke

There are no specific medical treatments for most causes of haemorrhagic stroke, except subarachnoid haemorrhage (see **Table 6.2**). All antiplatelet and anticoagulant drugs are stopped, and coagulation deficits are corrected. Monitoring of blood pressure and for increased ICP is needed.

Surgery

This is rarely indicated in ischaemic stroke. However, it may be lifesaving in a few clinical scenarios.

Acute ischaemic stroke

Early neurosurgical referral is indicated for posterior fossa and malignant middle cerebral artery infarctions.

Posterior fossa (cerebellar) infarction This can cause rapid neurological deterioration because of the small volume of space in the posterior fossa. It can also result in acute hydrocephalus and tonsillar herniation with brainstem compression.

Patients whose neurological examination indicates deterioration, and with hydrocephalus and brainstem compression, may benefit from surgical treatment to relieve hydrocephalus by cerebrospinal fluid diversion and subsequent decompressive surgery.

Malignant middle cerebral artery infarction Complete occlusion of the terminal internal carotid artery or main stem of the middle cerebral artery occurs in 10% of strokes. It results in massive middle cerebral artery territory stroke.

Within 48 h, patients develop severely increased intracranial pressure with cytotoxic oedema. Untreated, mortality is 80% with malignant cerebral oedema leading to intractable ICP elevation with subsequent brain herniation.

The results of a few studies have shown that decompressive hemicraniectomy (removal of part of the skull on the side of the infarction) decreases mortality, excess intracranial pressure and herniation (**Figure 6.7**). However, the effect on patients' quality of life is unclear.

Acute haemorrhagic stroke

All cases of haemorrhagic stroke require urgent discussion with a neurosurgeon.

In intraventricular haemorrhage, supportive measures such as cerebrospinal fluid diversion may be required. Patients with cerebellar haemorrhage may be treated conservatively or with surgery (either cerebrospinal fluid diversion via external ventricular drainage in isolation, or in combination with decompressive surgery). The choice depends on the degree of hydrocephalus and brainstem compression, and the patient's neurological status.

Patients with ruptured aneurysms or other intracranial arterial tears, ruptures and dissections urgently require surgical clipping, or endovascular intervention (e.g. coiling, stenting, vascular flow-diversion) (see *Section 6.4*).

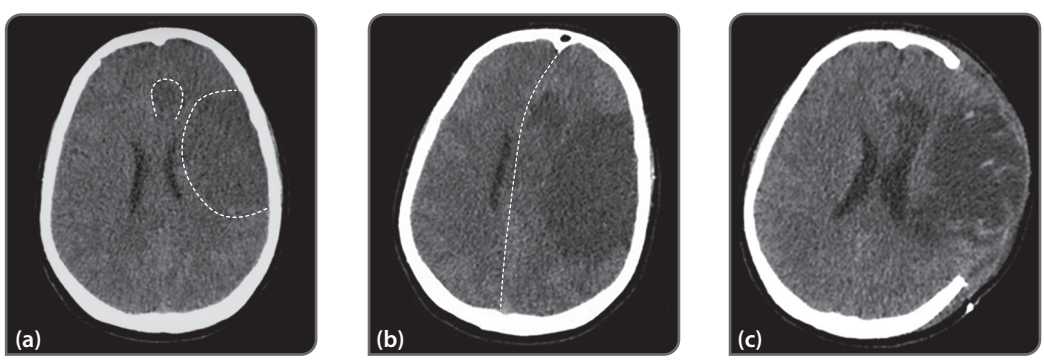


Figure 6.7 Malignant ischaemic infarction with subsequent decompressive craniectomy. (a) The initial CT scan demonstrates very early features that suggest an ischaemic event has occurred and there is a high risk of infarction. Note the subtle low-density changes occurring in the left cerebral hemisphere in comparison to the right side. The patient was alert at this point. (b) Only 36 h later, the patient's consciousness level deteriorated, they became obtunded and seizures developed. Repeat CT showed a more established infarct, with swelling and midline shift to the right (dotted line) and compression of the left lateral ventricle. (c) After decompressive hemicraniectomy, the midline shift had resolved, the ventricle was visible again and the swollen tissue has space to expand and protrudes from the skull defect. The decompression helps prevent life-threatening cerebral herniation from intractable intracranial pressure in elevation.

6.3 Transient ischaemic attack

In a transient ischaemic attack (TIA), the acute symptoms and signs of neurological dysfunction from a vascular occlusion resolve completely within 24 h. However, the occurrence of a 'mini stroke' suggests systemic atherosclerotic vascular disease and a high risk of major stroke:

- 15% of first strokes are preceded by TIAs
- 8–12% is the 7-day stroke risk after a TIA
- 18% is the 30-day stroke risk after a TIA.

Prompt investigation and intervention are essential. The latter includes secondary prevention, which reduces the 90-day stroke risk to:

- 10% if started within 3 weeks of a TIA
- 2% if started within 72 h.

Epidemiology

The annual incidence of TIA is 35 per 100,000 in the UK.

Aetiology

The causes of TIA are identical to those of 'ischaemic' strokes. The commonest causes are atherothromboembolism and cardioembolism.

Clinical features

As in a stroke, the features depend on the vascular territory affected. Most features resolve within 20 min. Systemic clinical examination is crucial to identifying aetiology. Listen for cardiac murmurs, assess for arrhythmias (especially atrial fibrillation) and auscultate for carotid bruit.

Amaurosis fugax is a common TIA syndrome caused by embolism occluding the retinal artery. A rapid, painless loss of vision in one eye is often described as 'a curtain coming down'.

Diagnostic approach

The aims of investigation are to identify the cause of the TIA and to define the degree of vascular risk. The ABCD2 score guides the urgency of investigation and implementation of secondary preventive measures against future TIAs and ischaemic strokes (**Table 6.8**).

Patients with suspected TIA should see a stroke specialist within 7 days. Those with ABCD2 score ≥4 are assessed ideally within 24 h. A score of ≥6 indicates a 35.5% risk of stroke within the next 7 days.

TIAs are investigated identically to an ischaemic stroke, with:

- imaging of the brain
- imaging of blood vessels (including the carotid arteries to assess for atherosclerosis)
- imaging of the heart (to assess for sources of cardiac emboli)
- blood tests.

Table 6.8 *ABCD2 risk score in the assessment of TIAs*

ABCD2	Criteria	Score
A	**A**ge ≥60 years	1
B	**B**lood pressure ≥140/90 mmHg	1
C	**C**linical features	2 if there is weakness 1 if there is a speech defect but no weakness
D	**D**uration of symptoms	2 if lasting ≥60 min 1 if lasting 10–59 min
D	**D**iabetes	1
The highest possible score is 7		

Management

Management aims to reduce the risk of stroke (secondary prevention).

Medication

Control of risk factors reduces not only stroke but also the risk of coronary and peripheral vascular disease:

- smoking cessation, weight loss, exercise and reduction in alcohol consumption
- control of hypertension (aiming for blood pressure <140/90 mmHg)
- optimisation of diabetes control
- control of hyperlipidaemia.

The second step is initiation of antiplatelet therapy.

- Aspirin 300 mg daily for 2 weeks, and then 75 mg of clopidogrel daily for life, reduce by 15–18% the risk of death associated with vascular disease
- Warfarin is indicated if the TIA was caused by cardioembolism and risk factors for cardioembolism are present (e.g. chronic non-valvular atrial fibrillation, metallic prosthetic cardiac valves and acute left ventricular wall motion impairment).

Warfarin is an extremely effective anticoagulant that significantly reduces stroke risk from cardiac embolism. However, it also increases the risk of haemorrhage (especially intracranial). Careful risk–benefit analysis, for example with the HAS-BLED prediction algorithm, is done before warfarin is started.

Surgery

In cardioembolism, surgery may be:

- cardiac electrophysiological ablation for atrial fibrillation
- valve repair or replacement for valvular disease.

Atheroma at the carotid bifurcation is the commonest cause of atherothromboembolism. If symptomatic, carotid endarterectomy may be indicated to remove the plaque. Carotid artery stenting is an alternative, but its long-term efficacy has yet to be established.

Prevention

Table 6.9 summarises the measures implemented in the primary prevention of stroke, i.e. preventing a first incidence of TIA or stroke.

Table 6.9 *Primary prevention of ischaemic stroke and TIA*

Risk factors	Rationale for intervention	Preventive measure(s)
Hypertension Smoking Diabetes Hyperlipidaemia	Precipitate atherosclerosis (by injury to vascular walls) and increase risk of atherothromboembolism	Lifestyle measures (e.g. smoking cessation, weight loss and exercise) Medical treatment of hypertension, diabetes and hyperlipidaemia
Cardiac embolism risk factors (e.g. non-valvular atrial fibrillation)	CHADS2 VASC score helps calculate this risk: **C**ongestive heart failure **H**ypertension **A**ge (<65 or >75 years) **D**iabetes Prior **S**troke or TIA **S**ex Other **VASC**ular disease	Aspirin alone may suffice for low-risk patients (i.e. those with atrial fibrillation, aged <65 years and with no other risk factors) In the absence of contraindications, warfarin is indicated in high-risk patients (e.g. those aged >75 years, with diabetes or with hypertension in association with atrial fibrillation)
Carotid artery atherosclerosis and stenosis	Carotid artery stenosis may be asymptomatic Stroke risk in asymptomatic stenosis is significantly lower than in symptomatic stenosis	Consideration for surgery (often a multidisciplinary team decision)

6.4 Cerebral aneurysms

An aneurysm is an abnormal localised 'ballooning' of a blood vessel. Rupture results in intracranial haemorrhage with significant morbidity and mortality. They are mostly in the anterior circulation (80–90%).

Types

Aneurysms consist of a neck and fundus, and are characterised by size, location and aetiology (**Figure 6.8**). They may be small (<1 cm in diameter), large (1–2.5 cm in diameter) or giant (>2.5 cm in diameter).

Epidemiology

The prevalence of intracranial aneurysms worldwide is approximately 6% with particularly higher prevalences in Asian and Finnish populations, and those who harbour significant risk factors (e.g. smoking, family history, hypertension).

Aetiology

Aneurysms can be developmental, inherited, infectious or traumatic.

- Developmental ('berry') aneurysms are the most common type; risk factors include hypertension, atherosclerosis and family history (up to 10% of people with two or more affected first-degree family members may have a developmental aneurysm)
- Aneurysms can develop in inherited diseases in which abnormal collagen (the key component of arterial walls) is formed (e.g. polycystic kidney disease, Marfan's syndrome and Ehlers–Danlos syndrome)

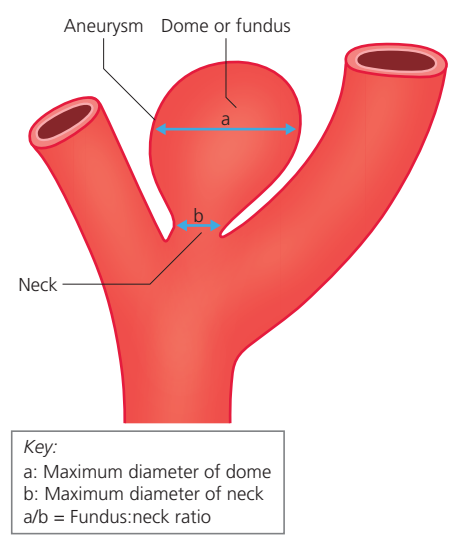


Figure 6.8 Structure of a typical intracranial aneurysm: the vessel wall is thinner where it has ballooned outwards to form an aneurysm at the branching point of two vessels. The fundus:neck ratio is often used, to evaluate the suitability of the aneurysm for interventional radiological treatment (endovascular coiling).

- Infectious ('mycotic') aneurysms are a rare complication of vessel wall inflammation resulting from infection
- Traumatic intracranial aneurysms (<1%) occur as a result of penetrating head injury.

The risk of aneurysm rupture is related to its size and is higher in smokers and patients with hypertension.

Pathogenesis

Multiple factors are implicated in the pathogenesis of cerebral aneurysm. They include a genetic predisposition to vessel wall weakness, for example in collagen deficiency, and precipitation by haemodynamic and metabolic stresses such as hypertension, smoking and diabetes.

Clinical features

Aneurysms usually present in one of three ways: rupture leading to haemorrhage, or focal neurological deficits secondary to compression of neural structures. Rarely, aneurysms may precipitate episodes of ischaemia as a result of vascular steal (blood flow diversion) or precipitating thromboembolic events (**Table 6.10**).

Diagnostic approach

Subarachnoid haemorrhage (**Figure 6.9**) is discussed in *Case 17.1* and in the subsequent section on differential diagnoses. Cerebral aneurysms, either symptomatic with rupture and subarachnoid haemorrhage or incidental, require non-invasive and invasive imaging to confirm diagnosis and define location and architecture.

- Non-invasive imaging techniques include CT angiography (**Figure 6.10**) and magnetic resonance angiography with three-dimensional reconstruction (**Figure 6.11**)
- Cerebral angiography with digital subtraction is invasive but is the gold standard and can be both therapeutic and diagnostic (**Figure 6.12**).

Management

Management of cerebral aneurysms depends on whether they are ruptured ('hot' aneurysm) or unruptured ('cold' aneurysm) and discovered incidentally or as a result of symptoms from mass effect.

Patients presenting with subarachnoid haemorrhage after aneurysm rupture

Patients with subarachnoid haemorrhage after aneurysmal rupture require immediate resuscitation and haemodynamic and neurological stabilisation, often in intensive care (see **Table 6.2**). Control of intracranial pressure and prevention of complications are critical (**Table 6.11**). The definitive form and timing of intervention to treat the cerebral aneurysm to prevent rebleeding is decided by taking into consideration the morphology and anatomical features of the aneurysm (fundus:neck ratio), its location, the patient's age and co-morbidities and if possible, the patient's own preference.

Any patient presenting with aneurysmal subarachnoid haemorrhage is at high risk of:

- rebleed
- vasospasm
- seizures
- hydrocephalus
- electrolyte disturbance.

If consciousness deteriorates, these must be excluded.

Patients with unruptured aneurysm

In these patients, the risk of future rupture and death is balanced against the risks of aneurysm repair in considering whether to intervene. Patient factors (age, co-morbidities and current

Table 6.10 *Clinical features associated with cerebral aneurysms*

Mechanism of presentation	Classification by location	Clinical features
Aneurysm rupture	Subarachnoid haemorrhage	Sudden-onset headache and meningism
	Intracerebral haemorrhage	Rupture can cause bleeding within a cerebral hemisphere with clot formation and focal neurological deficits
	Intraventricular haemorrhage	Acute hydrocephalus if aneurysm ruptures into ventricles causing obstruction to cerebrospinal fluid flow within
Focal neurological deficits (caused by compression)	Posterior communicating artery aneurysm	Fixed, dilated pupil unresponsive to light and accommodation as a result of CN III (oculomotor nerve) compression
	Aneurysm of segment of internal carotid artery in cavernous sinus	Cavernous sinus syndrome: eye movement abnormalities caused by compression of CNs III, IV and VI Facial pain and abnormalities of forehead sensation caused by compression of ophthalmic segment of CN V
	Anterior cerebral artery or anterior communicating artery aneurysm	Field defects caused by CN II (optic nerve) compression; the pituitary stalk may also be compressed with pituitary dysfunction from hypopituitarism
	Basilar artery aneurysm	Compresses brainstem structures with cranial nerve and long-tract signs/symptoms

CN, cranial nerve.

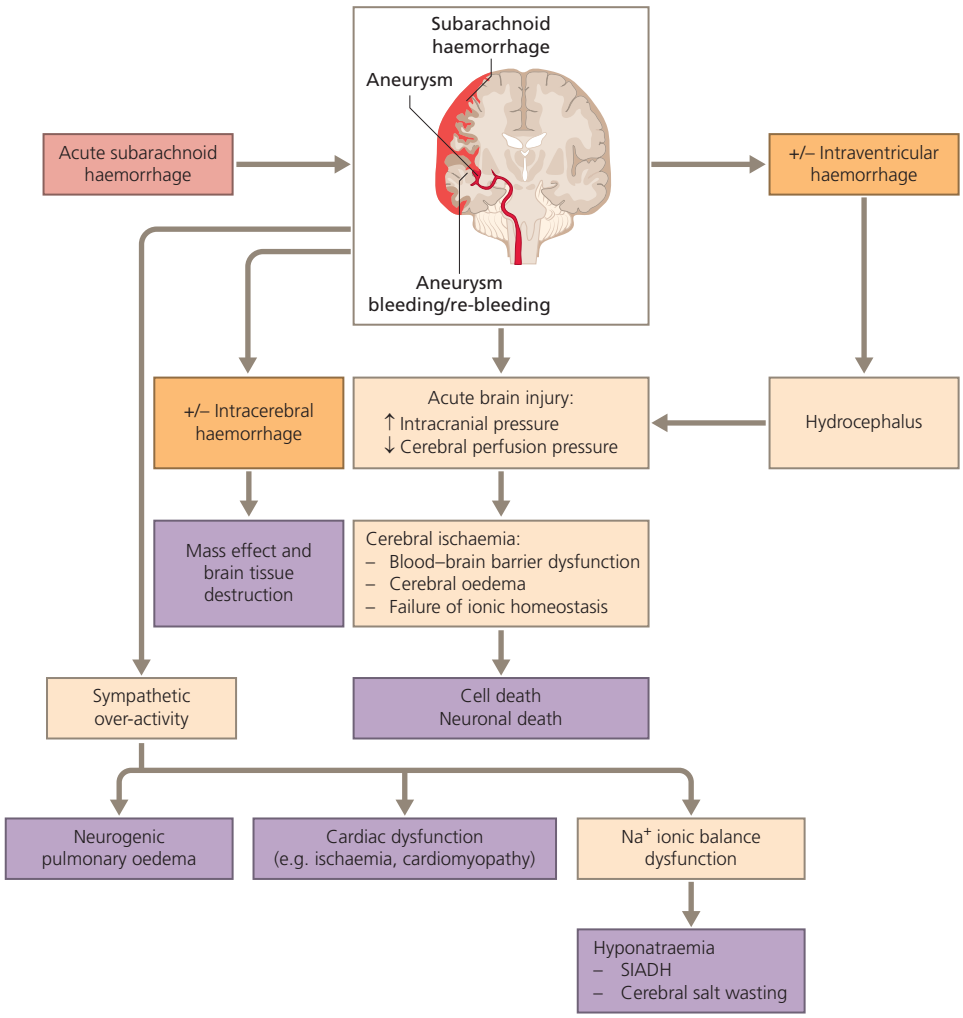


Figure 6.9 Pathophysiology of subarachnoid haemorrhage.

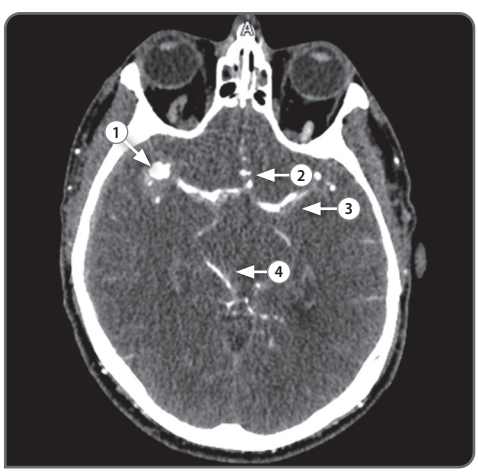


Figure 6.10 CT angiogram obtained after unenhanced CT had confirmed subarachnoid haemorrhage. CT angiography shows vasculature and is often the initial screening tool used to identify aneurysm as a cause of subarachnoid haemorrhage. ①, right middle cerebral artery aneurysm; ②, left anterior cerebral artery; ③, left middle cerebral artery; ④, terminal branches of the right posterior cerebral artery.

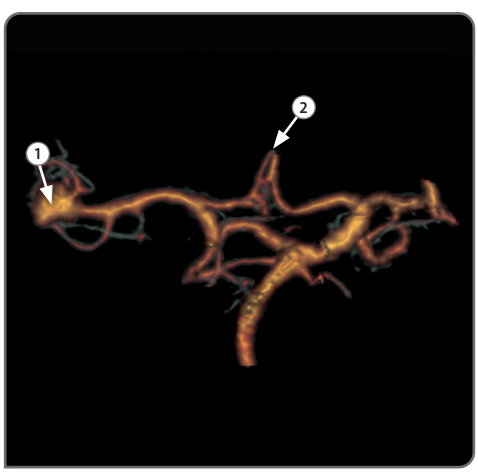


Figure 6.11 Three-dimensional reconstruction based on CT angiograms, showing a right middle cerebral artery aneurysm. These reconstructions are useful for measuring three-dimensional diameters of the aneurysm and for further planning of neurosurgical or neuroradiological intervention. ①, right middle cerebral artery aneurysm; ②, left anterior cerebral artery.

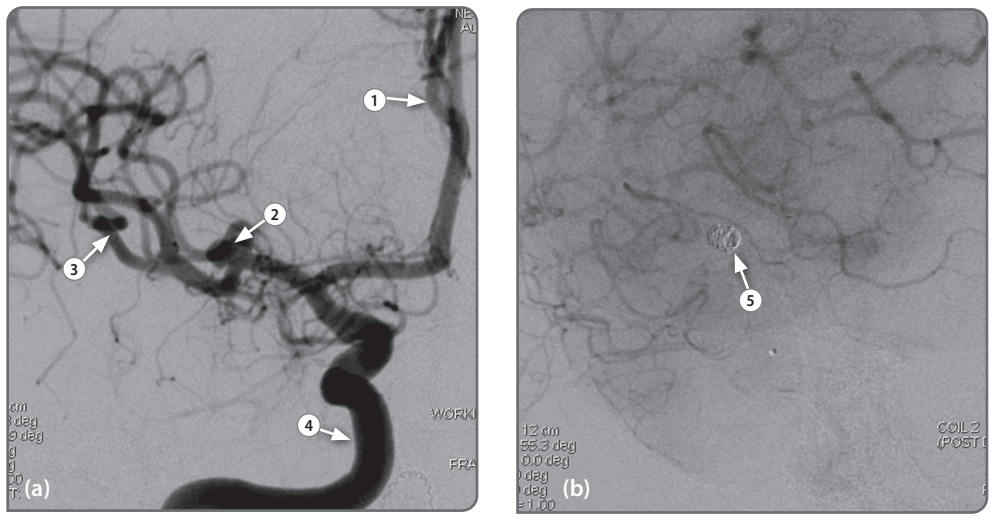


Figure 6.12 Antero-posterior (AP) cerebral catheter angiography (digital subtraction cerebral angiography) images before (a) and after (b) coil embolisation of an aneurysm. ①, anterior cerebral artery; ②, right middle cerebral artery aneurysm; ③, middle cerebral artery branches distal to the aneurysm; ④, right internal carotid artery; ⑤ coils occluding the aneurysm.

Table 6.11 ***Complications associated with aneurysmal subarachnoid haemorrhage***

Complication	Pathogenesis	Management and prevention
Rebleeding (30% risk on days 1–28 after untreated subarachnoid haemorrhage; 70% of patients die after rebleed)	It is unclear which ruptured aneurysms are at risk of early rebleeding Factors such as uncontrolled hypertension can precipitate re-rupture, as can a change in transmural pressures across the aneurysm wall (e.g. excess CSF drainage following external ventricular drainage to relieve acute aneurysmal subarachnoid associated hydrocephalus)	Definitive intervention to secure the aneurysm
Cerebral vasospasm or delayed ischaemic neurological deficit	Possibly a consequence of blood irritating cerebral vessels to cause vasospasm, with subsequent ischaemia and infarction	Reduce risk with nimodipine (60 mg every 4 h) for 21 days If symptomatic, increase blood pressure with intravenous fluids and inotropic and vasopressor agents (e.g. noradrenaline) – this is called 'triple H' therapy (hypertension, hypervolaemia and haemodilution); cerebral vessel dilating agents, e.g. intra-arterial papaverine, may be utilised along with endovascular intervention
Hydrocephalus	General subarachnoid haemorrhage obstructing arachnoid villi (communicating)	Initially amenable to lumbar punctures and cerebrospinal fluid drainage May require long-term CSF shunting
	Blood in ventricular system (non-communicating)	Requires external ventricular drainage of cerebrospinal fluid with external ventricular drain May require long-term CSF shunting
Seizures	Disruption of normal neuronal electrical activity	Anticonvulsant drugs
Hyponatraemia	Syndrome of inappropriate antidiuretic hormone secretion or cerebral salt wasting	Immediate discussion with intensive care and neurosurgeons

neurological symptoms) and aneurysm factors (size, morphology, location, operative difficulty and rupture risk) are considered. The decision is made jointly by the neurosurgeon, neuroradiologist and patient.

Definitive treatment of aneurysms

This requires neurosurgical clipping (**Figure 6.13**) or endovascular coiling (**Figure 6.14**) to block blood to the aneurysm and thereby prevent rupture and bleeding.

Clipping is associated with higher procedural morbidity than coiling; however, successful clipping usually provides a permanent cure. Coiling has a higher incidence of aneurysm regrowth and possible late recurrence with risk of re-rupture and subarachnoid haemorrhage.

Prognosis

About 15% of patients with subarachnoid haemorrhage from a ruptured aneurysm die before reaching hospital; 25% die within

24 h. Up to 40% die within the first month. Between 50 and 80% of patients who rebleed die within the first 24–48 hours.

Screening is recommended for people with two or more first-degree relatives with confirmed aneurysms. Counselling on the risks and benefits of identifying unruptured aneurysms is provided before screening. Diagnosis raises difficult decisions about relatively high-risk treatments, pregnancy (which increases the risk of rupture), life insurance, etc.

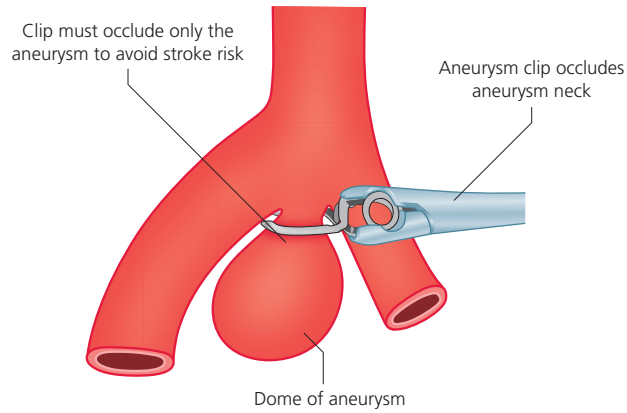


Figure 6.13 Principles of neurosurgical clipping. Craniotomy to open the skull facilitates exposure of the affected vessels. This allows a titanium clip to be passed around the aneurysm neck to occlude it. The clip is left in place permanently.

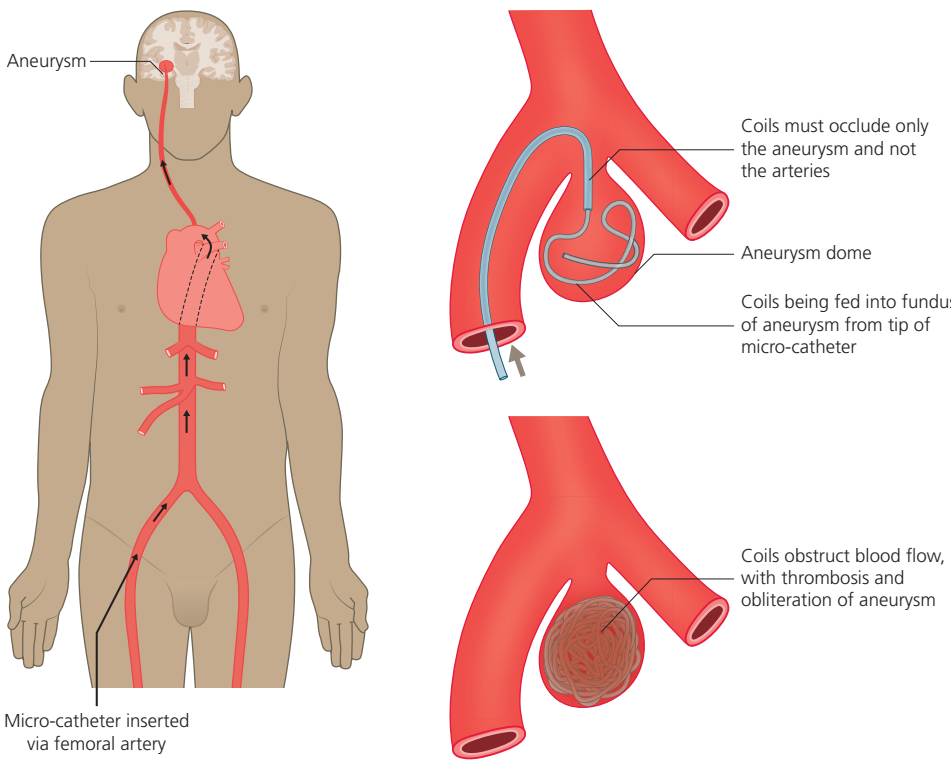


Figure 6.14 Endovascular coiling. A catheter tube is inserted, usually through the femoral artery, and passed via the aorta and carotid arteries to the neck of the aneurysm under radiographic guidance. Several platinum coils are delivered through the catheter to the aneurysm to occlude it.

6.5 Arteriovenous malformations

Arteriovenous malformations (AVM) are intracranial vascular anomalies of tangled masses of pial blood vessels (nidi). They have feeding arteries and draining veins. Blood is shunted directly from arteries to veins, bypassing the normal arteriole–capillary–venule network and thus causing complications. Many patients are asymptomatic, but symptomatic AVMs are associated with high morbidity and significant mortality.

Epidemiology

Arteriovenous malformations have an annual incidence of 1 per 100,000. Therefore, they are less common than aneurysms.

Aetiology

Most AVMs are congenital. They are multiple in some inherited syndromes, such as hereditary haemorrhagic telangiectasia.

Clinical features

Arteriovenous malformations may remain asymptomatic throughout life or manifest as intracranial haemorrhage, seizures or focal neurological deficits (**Table 6.12**).

Risk of haemorrhage is further increased if a patient has an aneurysm associated with AVM; this type of aneurysm can arise as a result of the increased pressure caused by shunting. The two types of AVM-associated aneurysm are:

- intranidal (in the AVM nidus)
- extranidal (in arteries feeding the AVM).

Diagnostic approach

CT or MRI angiography and cerebral angiography aid diagnosis. They also define AVM architecture for planning management (**Figures 6.15** and **6.16**).

Management

Management depends on patient factors, i.e. symptoms, age and co-morbidities, and AVM architecture, including nidus size, location relative to eloquent structures, pattern of venous drainage (superficial or deep) and presence of associated intra- or extranidal aneurysms (which potentially have an impact on risk of haemorrhage). The Spetzler–Martin grading system is used to stratify the operative risk associated with an AVM, based on its architecture.

Indications for intervention include expanding haemorrhage caused by AVM, progressive neurological deficits and high risk of haemorrhage (e.g. in a young patient with many years at risk).

Surgery

Three interventions are used, alone or in combination.

- Operative neurosurgical excision offers the best chance of cure after a single operation; small peripheral AVMs <3 cm in size in non-eloquent areas are ideal targets
- Stereotactic radiosurgery uses focused beams delivered in a single dose to obliterate small AVMs; obliteration takes up to 3 years, during which haemorrhage risk persists
- Interventional neuroradiology with embolisation occludes feeding vessels to reduce vascularity, and is a useful stand-alone treatment or pre- or post-operative adjunct to surgery or stereotactic radiosurgery; complications include haemorrhage and glue extravasation.

Treatment for AVM is extremely risky. Input from a multidisciplinary team, including a neurosurgeon and an interventional neuroradiologist, is critical in planning the optimal management strategy.

Table 6.12 *Clinical features associated with symptomatic AVMs*

Feature	Symptoms	Natural history
Haemorrhage (intracerebral or intraventricular)	Symptoms are variable and range from mild headache to focal neurological deficits to sudden collapse and death (depending on haemorrhage location, severity and associated complications, e.g. obstructive hydrocephalus)	Annual risk of 2–4% (if no previous haemorrhage history)
Epilepsy	Generalised or partial seizures	Risk higher after haemorrhage and in cortical AVMs
Focal neurological deficit	Symptoms depend on AVM location	Deficits result from mass effect, 'vascular steal' (diminished blood flow to non-AVM areas) or haemorrhage
Venous hypertension	Symptoms are those of increased intracranial pressure	Direct shunting from arteries increases venous pressure
Aneurysm formation	May result in subarachnoid haemorrhage	Caused by high pressures in blood vessels as a result of direct arterial–venous shunting. Can present in a similar manner as aneurysms without associated AVM (see **Table 6.10**)

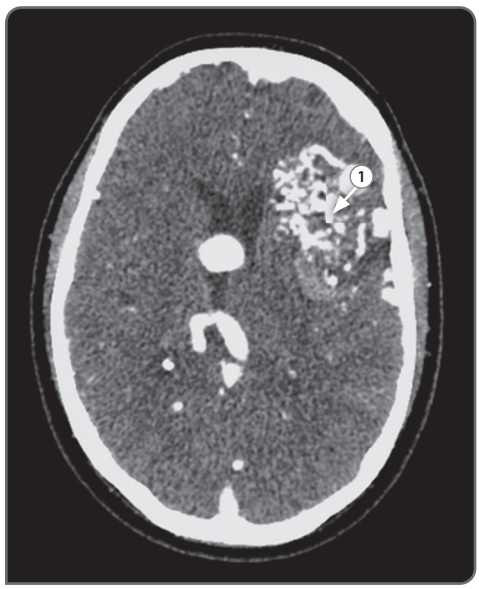


Figure 6.15 Axial post contrast CT images showing an irregular hyperdense area in the left frontotemporal regions after haemorrhage. The 'serpiginous' structures (1) filling up homogeneously with contrast represent dilated vessels and strongly suggest an underlying AVM.

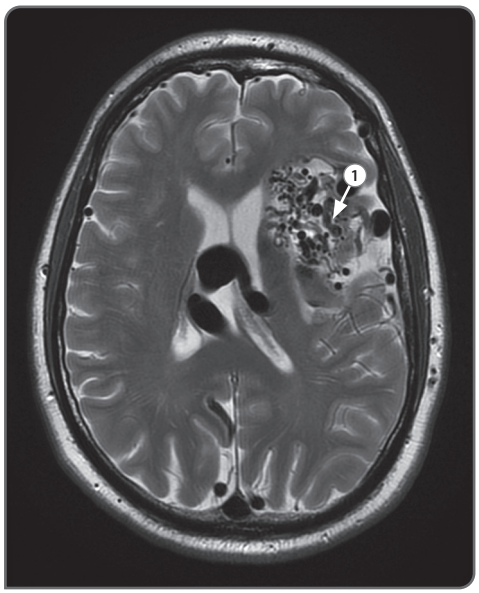


Figure 6.16 T2-weighted MRI showing multiple focal and serpiginous flow voids (1) (caused by flowing blood in the vessels) in the corresponding left frontotemporal regions. This finding confirms the AVM.

6.6 Cerebral venous sinus thrombosis

Superficial and deep cerebral veins and dural venous sinuses drain blood from the brain. Thrombosis in any of these venous structures precipitates infarction or haemorrhage in the territories they drain.

Epidemiology

The annual incidence of cerebral venous sinus thrombosis is 2 per 1 million people. Venous thrombotic infarction accounts for 1% of all strokes: 85% of these affect dural sinuses (superior sagittal sinus and transverse sinus), 10% affect deep cerebral veins and 5% affect the cavernous sinus.

Aetiology

The pathogenesis, and therefore the aetiology, is identical to that of arterial thrombosis and centres on Virchow's triad – any pathological process that affects a component of Virchow's triad can precipitate cerebral venous sinus thrombosis (see *Section 1.4.7*; **Table 6.13** provides examples of disorders that can precipitate venous sinus thrombosis classified according to the component of Virchow's triad they affect).

Clinical features

Headache, papilloedema, increased intracranial pressure, focal neurological deficits (e.g. hemiparesis and dysphasia) and seizures may occur.

Site-specific symptoms relate to underlying anatomy. For example, cavernous sinus thrombosis presents with defects of cranial nerves III, IV and VI as well as the ophthalmic division of cranial nerve V.

Diagnostic approach

Cerebral venous sinus thrombosis is a difficult diagnosis to make, because its clinical features are non-specific and it mimics other pathologies. A high index of suspicion is required. Cerebral venous sinus thrombosis must be confirmed or excluded through imaging. Potential causes are then explored and treated.

Investigations

CT and MRI scans can be normal, but they may show infarction in a region atypical for a specific arterial occlusion; the infarction is caused by increased venous pressure from the venous clot. The venous clot is occasionally visible with non-contrast CT, but it usually requires confirmation by the finding of filling deficits in the venous structures on CT or magnetic resonance venography (**Figure 6.17**).

Management

Treatment regimens vary and can be controversial.

Medication

The cause is treated, for example by immunosuppression for vasculitis, or cessation of precipitating drugs such as the combined

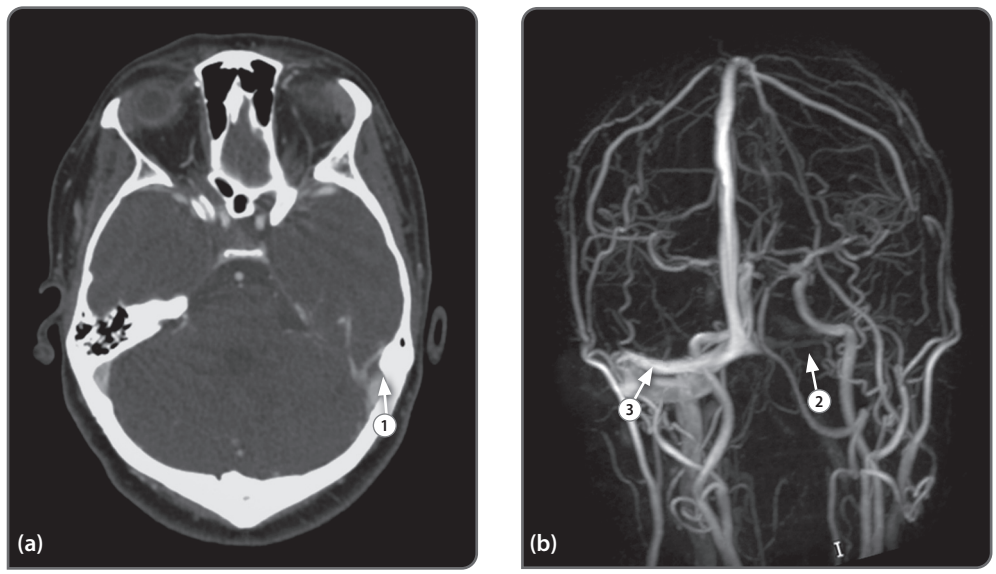


Figure 6.17 Venous thrombosis. (a) CT venogram, with arrow showing filling defect (dark hypodensity) in the left transverse sinus (empty delta sign) ① consistent with thrombosis in the left transverse sinus. (b) Magnetic resonance venogram showing absent flow in the left transverse and sigmoid sinuses, caused by occlusive thrombus ②, compared to the normally filling right transverse sinus ③.

Table 6.13 *Examples of the causes of central venous sinus thrombosis, classified according to Virchow's triad*

Abnormalities in blood constituents	Abnormalities in blood flow	Abnormalities in vessel wall
Drugs (e.g. combined oral contraceptive pill and hormone replacement therapy)	Venous stasis	Vasculitis (e.g. polyarteritis nodosa)
Infection or malignancy affecting face, eye, ear or nose	Dehydration	Intracranial infection (e.g. meningitis, HIV and abscess)
Malignancy (intra- or extracranial)	Pregnancy and puerperium	Inflammatory disorders (e.g. superficial lupus erythematosus and sarcoidosis)
Haematological disease (e.g. inherited thrombophilias and polycythaemia)		Iatrogenic venous injury during neurosurgery

These can be remembered easily based on the three principles of Virchow's triad, which underlies the pathogenesis of thrombosis and thrombus formation in any vessel.

oral contraceptive pill. Cerebral venous sinus thrombosis requires anticoagulation with heparin initially, followed by long-term warfarin. The duration of anticoagulation depends on the precipitating factor. The timing of anticoagulation initiation in the presence of a venous thrombosis associated haemorrhage is debated.

Surgery

This may be needed for intractable increases in intracranial pressure. Procedures include external ventricular drainage of cerebrospinal fluid and decompressive craniectomy.

Prognosis

Outcome varies according to severity of infarction and presenting consciousness level. Death is mainly the result of brain herniation from the increased intracranial pressure caused by diffuse infarction associated oedema, or haemorrhagic mass lesions.

6.7 Cavernous sinus syndromes

The cavernous sinuses are a pair of 2 cm venous blood-filled spaces either side of the pituitary gland. Critical structures traverse through each cavernous sinus, including cranial nerves (III, IV, VI and part of V) and the internal carotid artery. Diseases affecting the cavernous sinus produce a stereotypical clinical syndrome arising from compression and damage to these structures (**Figure 6.18**); permanent dysfunction may result.

Clinical features

A variety of diseases can affect the cavernous sinus including cavernous sinus venous thrombosis (due to infection, malignancy or idiopathic), infiltration by pituitary tumour, pituitary apoplexy and caroticocavernous fistulae (**Table 6.14**).

The following clinical features are common to and can occur with any pathological process that affects the cavernous sinus.

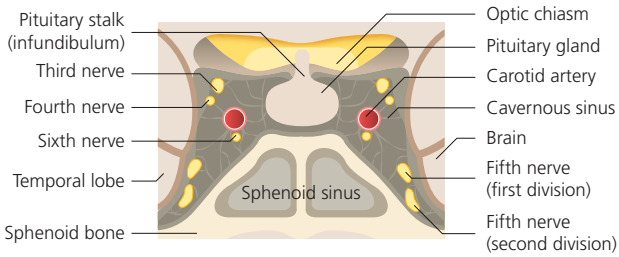


Figure 6.18 Coronal section through the cavernous sinuses, showing relationship to critical structures.

Painful eye movements and double vision may develop after palsies of cranial nerves III, IV and VI, and loss of forehead sensation when the ophthalmic division of cranial nerve V is affected. Eyeball protrusion (proptosis) and periorbital tissue oedema (chemosis) are common.

Ophthalmic vein dilatation and subsequent pressure-compression can lead to papilloedema, retinal haemorrhage, optic nerve atrophy and eventually loss of vision.

Pulsatile eyeball and cranial bruit (a 'whoosh' sound on eyeball auscultation) are often pathognomonic of a caroticocavernous fistula, an abnormal fistulous communication between the intracavernous portion of the internal carotid artery and the cavernous sinus.

Complications include spread of infection or malignancy to other intracranial sites in cavernous sinus thrombosis caused by infection or malignancy, respectively. Acute pituitary failure is a complication of pituitary apoplexy.

Management

Management is tailored to the cause (**Table 6.14**). Untreated, septic cavernous sinus thrombosis has 80% mortality from meningitis. This decreases to <20% with the use of appropriate antibiotics and occasionally surgical drainage.

The underlying aetiology often requires emergency intervention to prevent permanent damage to structures traversing the cavernous sinus, particularly:

- infections or malignancies near the eye, which require antibiotics and ophthalmological referral
- pituitary apoplexy, which warrants urgent neurosurgical referral for consideration of decompression to prevent visual failure.

Table 6.14 *Causes and management of cavernous sinus diseases*

Disease	Aetiology	Management
Cavernous sinus thrombosis	Idiopathic	Anticoagulation
	Ophthalmic or facial infection with intracranial spread	Antibiotics
	Extracranial malignancy from eye or facial region with intracranial spread	Referral to specialists
Pituitary apoplexy	Acute haemorrhage, usually associated with a pituitary tumour, and subsequent infarction of pituitary gland	Referral to neurosurgeon
	Idiopathic (e.g. anticoagulant use and Sheehan's syndrome*)	
Caroticocavernous fistula	Trauma to skull base	
	Rupture of aneurysm of intracavernous portion of internal carotid artery	

*Sheehan's syndrome is pituitary failure associated with postpartum haemorrhage causing pituitary necrosis.

6.8 Answers to starter questions

1. By definition, stroke requires the presence of neurological signs and symptoms. However, many people with risk factors for stroke (e.g. hypertension and diabetes) have evidence of damage to the brain but no symptoms. It is likely that this damage arose from the same process that occurs in clinical strokes. The brain may be so adaptable that in these people areas of it may be damaged without any clinical manifestation.
2. Treatments for stroke need to be given quickly to be as effective as possible. Intervention to restore circulation to ischaemic regions of brain is critical to limiting the size of the infarcted (dead) zone and saving the maximum amount of brain. This need for speed has led to national education programmes to educate the public on recognising stroke symptoms as early as possible.
3. TIAs can precede future strokes and indicate the presence of systemic atherosclerotic disease. Initiation of secondary prevention after a TIA greatly reduces the risk of subsequent strokes.
4. In adults, the regenerative capability of the brain is limited. Rehabilitation cannot reverse brain damage. However, it can help patients develop alternative strategies and techniques, such as the use of prostheses and occupational therapy aids, for carrying out their day-to-day activities. Rehabilitation is also crucial for maximising brain plasticity and avoiding complications following brain damage, such as treating contractures and spasticity. In children, the developing brain has an enormous amount of plasticity. After damage, it can develop new, different connections to replace lost brain function.