THE BARE ESSENTIALS

Stroke

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Stroke is a major public health problem because it is frequent, dangerous and expensive. Moreover, it can often be prevented, and may now be treatable in the acute stage. We will not cover subarachnoid haemorrhage here, which has a different clinical presentation and management from ischaemic stroke and spontaneous intracerebral haemorrhage (ICH), nor stroke rehabilitation.

EPIDEMIOLOGY

- **The incidence of stroke** is now higher than that of acute coronary syndromes. Patients with incident strokes are the target for acute stroke management (fig 1).
- Stroke is the **most prevalent neurological disorder** under the age of 85 years. Patients with prevalent stroke and transient ischaemic attacks (TIA) are the target for secondary prevention.
- Stroke is associated with **increased long-term mortality**, residual physical, cognitive, and behavioural impairments, recurrence, and increased risk of other types of vascular event, such as myocardial infarction.
- **The direct cost of stroke is high**, for instance in Germany the lifetime cost is about €40 000.

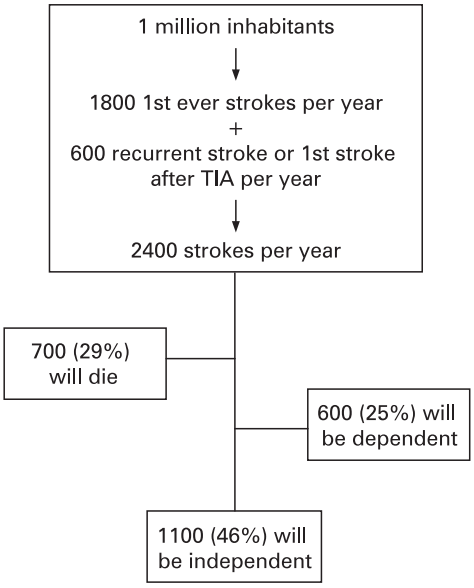

Figure 1 Epidemiology of stroke in a white population of 1 million.

IS THIS PATIENT HAVING A STROKE?

Stroke is characterised by a sudden or rapidly developing loss of cerebral function without any other cause than vascular, and includes both infarcts and haemorrhages. The classical definition requires the symptoms to last more than 24 hours, except in the case of early death. Although sometimes one or more are missing, the three clinical features suggesting a stroke are:

- **Sudden onset** of symptoms and signs, either all at once within seconds or developing over a few minutes, and often worsening over the next minutes or hours, then stabilising and improving over time.
- **Focal symptoms and signs**, that is, generally explained by a single lesion in the brain (boxes 1 and 2). Note: the symptoms and signs may not necessarily be explained by a single lesion when the patient has already had a stroke, or develops several acute strokes in different territories.
- **"Negative" symptoms**, that is, suggesting loss of function. Symptoms may (rarely) be "positive"—for example, jerking of a limb, seizure, paraesthesia, seeing flashing lights, visual hallucinations, or movement disorders.

HOW SEVERE IS THIS STROKE?

The level of consciousness can be assessed with the Glasgow Coma Scale (GCS). Its main limitations in stroke are when there is aphasia or a motor deficit (the best motor response should then be evaluated in non-paretic limbs).

The severity of the neurological deficit can be assessed by the National Institutes of Health (NIH) Stroke Scale which quantifies different categories of neurological impairments, including consciousness. It is widely used in monitoring stroke patients and as a selection criterion for thrombolytic therapy. Although it takes only minutes, is reliable and reproducible, and can be performed by a non-neurologist, some training is still required (http://www.ninds.nih.gov/doctors/NIH_Stroke_Scale.pdf)

WHAT TYPE OF STROKE IS IT?

Intracerebral haemorrhage accounts for about 10% of all strokes in white populations, and presents in much the same way as ischaemic stroke. Although some symptoms are more frequent in ICH (for example, headache, impairment of consciousness

Box 1 Focal neurological symptoms consistent with the diagnosis of stroke

- Motor symptoms: weakness or clumsiness of one side of the body (hemiplegia or hemiparesis), or part of one side of the body.
- Sensory loss: decreased sensation on one side of the body, or part of one side of the body.
- Aphasia: impairment or loss of linguistic abilities, resulting in difficulties speaking, understanding conversation, reading or writing.
- Visuospatial neglect: usually on the left side and associated with left hemiplegia and hemianopia.
- Visual disturbances: monocular blindness, hemianopia or quadrantanopia, bilateral blindness with anosognosia.
- Other focal symptoms that may suggest a stroke, but only in the right context, usually with other focal symptoms
  - dysphagia
  - ataxia
  - paraparesis or paraplegia
  - dysarthria
  - diplopia
  - rotational vertigo
  - acute unilateral hearing loss
  - acute amnesia.

at onset, epileptic seizures), none is specific enough for diagnosis in an individual patient. Brain imaging is mandatory to differentiate ischaemic stroke from ICH. This is crucial because ICH and ischaemic stroke patients require different diagnostic work-up, acute treatment and secondary prevention.

When an MR scan is available in an emergency

- **T1- and T2-weighted images, and FLAIR** sequences to identify old lesions and lesions of non-vascular origin.
- **Diffusion weighted images (DWI)** to identify new ischaemic lesions (fig 2). Low cerebral blood flow induces cytotoxic oedema with cellular swelling and, as a consequence, decreased movement of extracellular water which is responsible for the hyperintense signal on DWI and a decrease in the apparent diffusion coefficient of water (ADC). These changes appear before those on T1, T2 and FLAIR sequences.
- **T2* sequences** to identify haemorrhages (fig 3) and brain microbleeds.
- **Time-of-flight sequences** to show occlusions of the extra- and intracranial arteries (fig 4).
- **Perfusion-weighted images (PWI)** may be useful to show the area at risk in cerebral ischaemia.

Box 2 Non-focal neurological symptoms, which do not suggest a stroke or transient ischaemic attack, except when they are associated with focal neurological symptoms

- Generalised weakness
- Light-headedness, syncope, faintness, non-specific dizziness
- Confusion
- Incontinence
- Drop attack
- Tinnitus

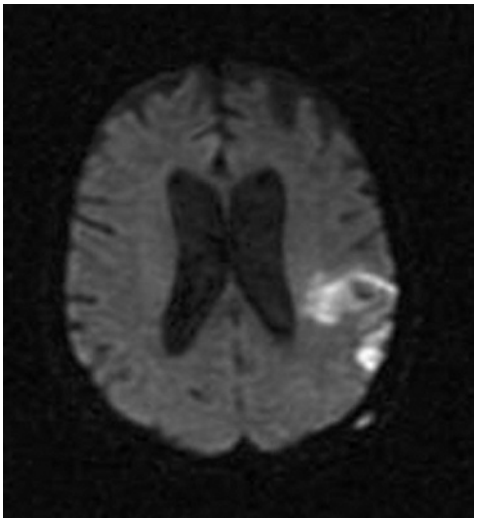

Figure 2 MR brain scan in the acute stage of cerebral ischaemia (DWI sequence). Left middle cerebral artery infarct showing ischaemic lesions in the cortex and subcortex as bright signal.

When an MR scan is not available in an emergency

There are contraindications to MRI (pacemaker, claustrophobia, agitation etc.), and it is not available everywhere. In these situations, a brain CT-scan without contrast should be performed, mainly to differentiate ICH (hyperdensity in the

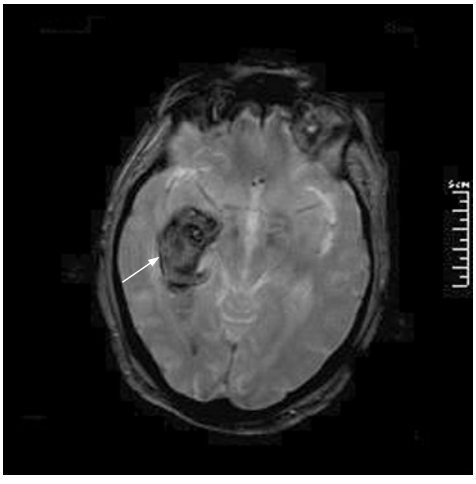

Figure 3 MR brain scan in the acute stage of a right temporal intracerebral haemorrhage (T2* sequence) (arrow).

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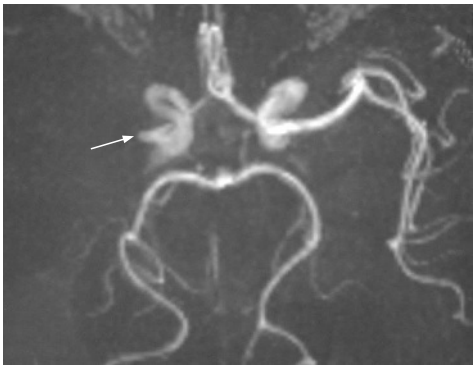

Figure 4 MR angiography in the acute stage of cerebral ischaemia (time of flight sequence) showing occlusion of the main stem of the right middle cerebral artery (arrow).

brain parenchyma) from ischaemic stroke, and to diagnose structural mimics of stroke (subdural haematoma, tumour etc).

In acute cerebral ischaemia, the scan may be normal—especially very early—but there may be signs of cerebral ischaemia, even within three hours: loss of the limits of the lenticular nucleus, loss of the insular ribbon, disappearance of the difference between grey and white matter. When the middle cerebral artery is occluded, the CT scan may show it as hyperdense. New generation CT scanners can now provide arterial anatomy and perfusion information, but this requires irradiation and intravenous contrast.

WHERE IS THE LESION?

In most cases an MR-scan localises the lesion in an emergency. However, it is still crucial to determine the location by clinical evaluation because:

- **MRI may not be available**, and CT scans are often normal in cerebral ischaemia, especially very soon after onset, and in minor strokes or TIA.
- **Clinical evaluation** may find signs that cannot be explained by the lesion seen on MR, suggesting another, invisible lesion.

The Oxfordshire Community Stroke Project classification of stroke syndromes, based on easily observed clinical features, has good positive and negative predictive values against brain imaging once the stroke lesion is complete, and before any of the signs have resolved:

- **Lacunar syndromes (LACS)**:
  - no visual field defect
  - no new disturbance of higher cortical or brainstem function
  - pure motor hemiparesis, or pure sensory deficit of one side of the body, or sensory-motor hemiparesis, or ataxic hemiparesis (dysarthria clumsy hand syndrome or ipsilateral ataxia with crural hemiparesis)
  - at least two of the three areas (face, arm, leg) should be involved, and the limb should be involved in its entirety.
- **Posterior circulation syndromes (POCS), any one of:**
  - cranial nerve impairment
  - unilateral or bilateral motor or sensory deficit
  - disorder of conjugate eye movement
  - cerebellar dysfunction
  - homonymous hemianopia
  - cortical blindness.
- **Total anterior circulation syndromes (TACS):**
  - hemiplegia and homonymous hemianopia contralateral to the lesion, *and*
  - either aphasia or visuospatial disturbance
  - ± sensory deficit contralateral to the lesion.
- **Partial anterior circulation syndromes (PACS):**
  - one or more of unilateral motor or sensory deficit, aphasia or visuospatial neglect (combined or not with homonymous hemianopia)
  - motor or sensory deficit may be less extensive than in lacunar syndromes (for example, hand alone).

TRANSIENT ISCHAEMIC ATTACKS

The classical definition is an acute loss of focal cerebral or monocular function with symptoms lasting less than 24 hours, with no other explanation than an inadequate blood supply. In practice most TIAs last only a few minutes and many brain TIAs have an appropriate lesion on brain imaging, more often with MR than CT. Of course at onset, one cannot predict which patient will continue to have symptoms for more than 24 hours (that is, a stroke) and so at this stage it is best to diagnose a "brain attack". The major difficulty with TIA patients (and sometimes physicians) is that, often, they do not consider the symptoms as an emergency, because they resolve. This is an important issue because some of these patients have a high risk of ischaemic stroke, and half the patients who do have a stroke after a TIA do so within a week and some are preventable. Like strokes, TIAs are an emergency, at least when seen within the first few days.

Differential diagnosis of TIA (and often stroke)

- **Migraine aura**: the first episode occurs generally between 15 and 20 years of age, with a family history, and usually consists of "positive" (visual or sensory) symptoms, which develop over 5–20 minutes to maximum severity, and last for less than one hour, usually but not always followed by headache. Migraine may be associated with the cause of stroke/TIA (for example, CADASIL, familial amyloid angiopathy, mitochondrial cytopathies).

- **Focal epilepsy**: post ictal paralysis may be confused with a TIA if the seizure has not been identified, while sometimes there is limb shaking during a TIA.
- **Transient global amnesia** occurs at the same age as TIA/stroke, is of sudden onset, and spontaneously recovers in a few hours, but the history—necessarily from a witness—of amnesia without other symptoms (apart sometimes from headache) is very characteristic.
- **Structural brain lesions** may mimic a TIA or stroke: for example, chronic subdural haematoma, meningioma, intracranial venous thrombosis, etc (all easily identified by brain imaging).
- **Hypoglycaemia** is usually associated with hunger, dizziness, palpitations, sweating and confusion—but not always, and the symptoms can be focal.
- **Multiple sclerosis** may start with focal symptoms of sudden or rapid onset, but usually in a much younger age group.
- **Labyrinthine disorders** with isolated vertigo and sometimes hearing loss or tinnitus may be misdiagnosed as a TIA or stroke.
- **Mononeuropathies** may be misdiagnosed as TIAs, or even strokes, particularly when transient.

WHAT IS CAUSING THIS STROKE OR TIA?

Ischaemic strokes and TIA

In white populations the most frequent causes are large-artery atherosclerosis (about 50%), atrial fibrillation (about 25%), and small vessel disease of the deep perforators (about 20%), and in young patients the leading cause is arterial dissection (box 3). In other populations the causes are somewhat different, particularly valvulopathies and infectious disorders. In all patients the following are necessary:

- **Clinical examination**, especially for cardiac abnormalities and arterial pulses/bruits.
- **Full blood count** to detect polycythaemia and thrombocythaemia.
- **Raised erythrocyte sedimentation (ESR) or C-reactive protein** to detect vasculitis, infections, etc.
- **Blood glucose** to detect diabetes, or hypoglycaemia in the acute situation.
- **Urea and electrolytes** (baseline) and **blood cholesterol** (risk factor).
- **ECG** to detect atrial fibrillation and acute myocardial infarction.
- **Cervical artery ultrasonography** to detect stenosis or occlusion, or dissection.
- **Optional investigations** are guided by the results of the initial investigations, age, and the clinical context:
- **Angiography** (MR, CT or catheter).
- **Transthoracic echocardiography** to detect intracardiac thrombus or tumours, valvulopathies, valvular vegetations, decreased ventricu-

Box 3 Causes of ischaemic strokes and TIAs

Large-vessel atherosclerosis
- Cervical arteries (internal carotid artery, vertebral artery, subclavian artery)
- Intracranial extracerebral arteries (middle, anterior, posterior, vertebral and basilar arteries, Circle of Willis)

Embolism from the heart
- High-risk conditions
  - atrial fibrillation
  - mitral stenosis
  - acute myocardial infarction
  - intra-cardiac thrombus
  - cardiac tumours (myxoma, fibroelastoma)
  - infectious endocarditis
  - marantic endocarditis
  - cardiac catheterisation or surgery
  - mechanical prosthesis
- Low-risk conditions
  - tissue prosthesis
  - patent foramen ovale +/− interatrial septal aneurysm
  - isolated inter atrial septal aneurysm
  - mitral valve prolapse
  - dilated cardiomyopathy

Intracranial small-vessel occlusion
- Small vessel disease of the deep perforators
- Genetic disorders of the deep perforators
  - CADASIL
  - CARASIL
  - non-notch 3 familial small-vessel occlusions

Other definite causes
- Dissection
  - cervical arteries
  - intracranial arteries
  - aortic arch
- Vasculitis
  - Secondary, eg infectious, systemic inflammatory disorders
  - primary angiitis of the central nervous system
- Angiopathies
  - vasoactive: migraine, postpartum angiopathy, prescription drugs, illicit drugs, snake bite
  - irradiation
  - fibromuscular dysplasia
- Metabolic disorders
  - MELAS
  - Fabry's disease
  - oxalosis
  - homocystinuria
- Rare types of emboli
  - fat embolism
  - gas embolism
- Haematological disorders
  - polycythaemia rubra vera
  - thrombocythaemia
  - leukaemia
  - thrombophilias
  - sickle cell disease
- Intracranial vascular malformations

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lar ejection fraction, patent foramen ovale (transoesophageal echocardiography if necessary).
- **24-hour ECG** if intermittent arrhythmia suspected.
- **Specialised biological tests** when a specific cause is suspected, such as antinuclear and anticardiolipin antibodies, syphilis serology, etc.

Intracerebral haemorrhage

The causes of ICH are listed in box 4; most cases not due to an intracranial vascular malformation are due to small-vessel disease (a consequence of chronic arterial hypertension) or cerebral amyloid angiopathy (generally lobar haemorrhage). In all patients the following are necessary:

- **Careful history** for hypertension, medications, alcohol consumption, family history of stroke, cancer, trauma, illicit substance use.
- **MRI** may show cavernous malformation, intracranial venous thrombosis, brain microbleeds, arteriovenous malformation, tumour, signs of unrecognised trauma (brain contusions, scalp haematoma, etc).
- **Coagulation tests**.
- **Blood pressure** recordings, remembering blood pressure increases as a consequence of ICH.
- Search for relevant **illicit drugs** in blood and urine.
- **Magnetic resonance- or CT- or catheter angiography** depending on age, history of arterial hypertension, and location of the ICH:
  - young patient
  - no hypertension
  - ICH not in one of the usual sites for small vessel disease (that is, not putamen, globus pallidus, thalamus, internal capsule, deep periventricular white matter, pons, and cerebellum).

In clinical practice, ICHs are usually under-investigated: the concept of "primary" ICH should be abandoned or at least revised, and a cause carefully considered in every case.

RISK FACTORS FOR STROKE

As well as non-modifiable risk factors (increasing age, male gender, and familial predisposition), other risk factors can be modified and if on the causal pathway are targets for stroke prevention:

- **Blood pressure**: there is a continuous and causal linear relationship between usual systolic and diastolic blood pressure and the incidence of both ischaemic and haemorrhagic stroke, at any age, in both genders, without any threshold. The risk of stroke doubles for every 7.5 mm Hg increase in diastolic blood pressure.
- **Blood cholesterol**: there is a somewhat increased risk of ischaemic stroke with increasing total and LDL cholesterol levels, and decreasing HDL cholesterol. Many patients with ICH have normal or even low cholesterol levels.
- **Cigarette smoking** doubles the risk of ischaemic stroke.
- **Diabetes mellitus** doubles the risk of ischaemic stroke, independently of other factors.
- **Oral contraceptives**:
  - low oestrogen pills (<50 μg) are associated with a low risk of ischaemic stroke, in the absence of any other vascular risk factor
  - high oestrogen pills (≥50 μg) are associated with a higher risk of ischaemic stroke
  - the attributable risk of stroke in young women using oral contraceptives is very low, about 1 per 200 000 woman-years
  - there are no clear data for progestogen-only pills
  - even at low doses, the risk of intracranial venous thrombosis is increased.
- **Hormone replacement therapy** increases the risk of ischaemic stroke and should be avoided in postmenopausal women with ischaemic stroke/TIA.

Box 4 Causes of non-traumatic intracerebral haemorrhage

Vascular malformations
- arteriovenous malformation
- cavernous malformation
- dural arteriovenous fistula
- saccular aneurysm
- moyamoya syndrome

Morphological abnormalities of the cerebral arteries
- small vessel disease of the deep perforators
- cerebral amyloid angiopathy
- CADASIL
- intracranial dissection
- vasculitis
- mycotic aneurysm

Intracranial venous thrombosis

Brain tumours
- metastasis
- primary malignant brain tumours

Haemostatic disorders
- iatrogenic: thrombolytic therapy, oral anticoagulation, antiplatelet agents
- congenital or acquired coagulation disorder: haemophilia, thrombocytopenia

THE OUTCOME AFTER STROKE

Any type of stroke (ischaemic and haemorrhagic)

Short-term outcome:

- **Early epileptic seizures** (<2 weeks after stroke onset) occur in about 5% of patients, more likely with a cortical lesion and a more severe stroke.
- **Delirium** occurs in one quarter of stroke patients, more frequent in those with

pre-existing cognitive decline and who develop metabolic or infectious complications.

- Large cerebellar strokes may lead to **hydrocephalus** or direct **compression of the brainstem**, usually between 48 and 96 hours in infarcts, earlier in haemorrhages.
- **Non-specific complications** include pressure sores, pneumonia, urinary tract infection, hyponatraemia, deep venous thrombosis and pulmonary embolism. They are all more frequent in patients with severe neurological deficits.

Long-term outcome:

- **Dementia** is a major cause of dependency after stroke; in about 30%. Post-stroke dementia may be due to any combination of vascular lesions, Alzheimer pathology and leukoaraiosis.
- **Post-stroke depression** occurs in up to half of stroke survivors and remains high over time.
- **Late epileptic seizures** (>2 weeks after stroke onset) occur in about 4% of patients, particularly with cortical lesions, severe strokes, and associated dementia.
- **Physical sequelae** (motor or sensory deficits, pain, hemianopia) and neuropsychological deficits (aphasia, neglect, emotionalism, anxiety) are other major components of post-stroke disability.

Ischaemic stroke

- Malignant infarcts with swelling and raised intracranial pressure occur mainly (but not exclusively) in young patients with large hemispheric infarcts, usually within 48 hours of onset, and have a high case fatality.
- Spontaneous haemorrhagic transformation occurs even in the absence of antithrombotic or thrombolytic drugs, and may or may not increase stroke severity.
- The risk of early (and later) recurrence declines with time and depends mainly on stroke severity (the greater the severity the lower the risk) and cause (high in atrial fibrillation or severe carotid stenosis, low in dissection).
- New ischaemic events in other vascular territories are also frequent (myocardial infarction, aortic dissection, etc).

Transient ischaemic attacks

- **Ipsilateral stroke** risk is high, especially early: on average 8% at one week, 12% at one month, and 17% at three months. The six-point "ABCD" score (box 5) predicts the seven-day risk of stroke: score <5: 0.4%; score = 5: 12%; score = 6: 31%.

The early risk of stroke also depends on the underlying cause: 4% at one week and 13% at one month for large-artery atherosclerosis, but only 0% and 2% respectively in lacunar ischaemic stroke.

- **Other vascular events**: there is a high risk of myocardial infarction (2% per year) and non-stroke vascular death (2% per year), both stable over time.

Box 5 Six-point "ABCD" score for predicting one week stroke risk after a transient ischaemic attack

Age (years)
- ⩾60 = 1
- <60 = 0

Blood pressure
- systolic >140 mm Hg and/or diastolic ⩾90 mm Hg = 1
- systolic ⩽140 mm Hg and diastolic <90 mm Hg = 0

Clinical features
- unilateral weakness = 2
- speech disturbance without weakness = 1
- other = 0;

Duration of symptoms (min)
- ⩾60 = 2
- 10–59 = 1
- <10 = 0

Intracerebral haemorrhage

- **30-day case fatality** increases with:
  - volume of haematoma (93% for deep ICH>60 cm^3, 7% for lobar ICH<30 cm^3)
  - decreasing Glasgow Coma Score
  - increasing age
  - infratentorial location
  - intraventricular bleeding
  - hydrocephalus.
- **Secondary growth** of ICH occurs in about one quarter of patients after 4 hours, and in one third after 24 hours, and may be the consequence of continuous bleeding, or rebleeding. ICH growth is associated with clinical worsening.

The risk of stroke recurrence after ICH has probably been underestimated in the past: the annual risks are about 2% for recurrent ICH and 1.4% for ischaemic stroke.

HOW CAN WE REDUCE DEATH AND DEPENDENCY?

Non-specific management

- **Detection and management of life-threatening emergencies** (aspiration, status epilepticus, respiratory arrest, etc).
- **Stabilisation of physiological parameters** (hypoxaemia, hyperglycaemia, hyperthermia, decreased cardiac output, and dyhydration), especially during the first days, with the exception of blood pressure because there is transient loss of autoregulation of cerebral blood flow. Therefore, although there are no evidence-based data, high blood pressure

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should not be treated in the acute stage unless there is an associated life-threatening disorder such as aortic dissection or ICH (see below).

- **Early prevention of complications**:
  - Pressure sores: appropriate caloric intake, early mobilisation and appropriate beds and nursing.
  - Aspiration pneumonia: detection of swallowing impairment and nasogastric tube when necessary.
  - Deep venous thrombosis and pulmonary embolism: low molecular weight heparin reduces the risk but has no *overall* effect on mortality (because it increases the risk of intracranial and extracranial bleeding).
  - Rehabilitation can be started as soon as the patient is stable: passive measures minimise the risks of contractures, pressure sores and pneumonia.
  - Stroke unit care provides coordinated multidisciplinary input, with continuous training of specialised staff members, and reduces mortality and dependency, in part by the prevention of non-specific complications that occur in the first days.

Specific management of ischaemic stroke

Antithrombotic therapy

- **Aspirin** 300 mg at once and then 75–150 mg daily prevents 15 dependencies or deaths per 1000 patients treated. Because of the large number of patients who can receive aspirin, this small individual effect provides a reasonable benefit in terms of public health. Aspirin should not be started until 24 hours after any thrombolysis.
- **Unfractionated or low-molecular weight heparins** do not provide any overall benefit because the decreased early ischaemic recurrences are counterbalanced by haemorrhagic transformations. There is no reason to recommend heparin routinely during the acute stage of ischaemic stroke, even in patients with atrial fibrillation.

Thrombolytic therapy

- **Intravenous recombinant tissue plasminogen activator (rt-PA)** increases the odds of a favourable outcome at 3 months by about eight times if given within 90 minutes of onset, and by about twice within 91–180 minutes. Case fatality is not affected if given up to 270 minutes, but increases thereafter. Haemorrhagic transformation is associated with increasing age, and large infarcts. The main messages are the sooner rt-PA is given, the greater the benefit, and there may be potential benefit beyond 3 hours, but with some risks.
- **The dose** is 0.9 mg/kg (10% as an iv bolus, then 90% as a continuous iv injection over 1 hour), contraindications are listed in box 6.
- **Other ways to achieve early recanalisation** are currently under investigation: other thrombolytic drugs, intra-arterial thrombolytic therapy, mechanical devices, and ultrasound-assisted iv thrombolytic therapy.

Neuroprotection

- **Neuroprotective drugs** that have shown an effect in animals have so far failed in humans.
- **Hypothermia** is a potential way to achieve neuroprotection but, because of adverse effects and the need for intensive care, can only be used in severe cases, especially for patients at risk of malignant infarcts.

Surgery

- In large cerebellar infarcts with hydrocephalus or brainstem compression, **ventricular drainage or posterior fossa decompression** are recommended, although these interventions have never been tested in randomised trials.
- **Decompressive hemicraniectomy** reduces mortality and disability in patients with large infarcts in the middle cerebral artery territory, but it is difficult to know exactly when to intervene.

Box 6 Contraindications to iv thrombolysis in acute cerebral ischaemia

- Age <18 years
- No motor deficit
- Symptom onset >3 hours
- NIH stroke scale >25 or <4
- Impaired consciousness
- Recent epileptic seizure
- History of intracerebral haemorrhage or vascular malformation
- Known coagulopathy
- Pregnancy or breastfeeding (not menstruation)
- Lumbar puncture or any arterial puncture at a non-compressible site <7 days
- Major surgery or delivery <15 days
- Gastrointestinal bleeding <21 days
- Myocardial infarction <21 days
- Pericarditis <3 months
- Head trauma <3 months
- Any current treatment with heparin or oral anticoagulation
- Possible endocarditis (temperature >37°5+ cardiac murmur)
- Possible aortic dissection
- Systolic blood pressure >185 mm Hg, diastolic blood pressure >110 mm Hg
- Blood glucose <3 mmol/l or >22 mmol/l
- International normalised ratio (INR) >1.5; or activated cephalin time (ACT) >40, or platelets <100 000/mm^3

Specific management of intracerebral haemorrhage

Blood pressure management

Reducing blood pressure in acute ICH may prevent haematoma growth and decrease the risk of rebleeding, but also reduces perfusion pressure and may compromise cerebral blood flow. Based on these considerations rather than any randomised trials:

- **For patients with known prior hypertension or signs of chronic hypertension**, an upper limit of systolic blood pressure of 180 mm Hg and a diastolic blood pressure of 105 mm Hg is recommended before treatment is necessary; the target blood pressure should be 170/100 (or a mean blood pressure of 125 mm Hg).
- **For patients without known hypertension**, the upper recommended limits are 160/95 mm Hg before treatment is necessary; the target should be 150/90 (or a mean of 110 mm Hg).
- **Intravenous labetalol, enalapril, or urapidil** are the most widely used drugs. Sodium nitroprusside is sometimes necessary but has major adverse effects such as tachycardia, coronary ischaemia, antiplatelet action, and increasing intracranial pressure.

Prevention of deep venous thrombosis

- **Graded compression stockings** are effective in surgical patients, but their efficacy in stroke patients when they can only be fitted *after* the initiating event is still being tested.
- Although subcutaneous **unfractionated and low molecular weight heparins** reduce venous thromboembolism, their effect is counterbalanced by an increase in haemorrhagic complications.

Increased intracranial pressure

- The main methods of **medical decompression** include hyperventilation, osmotic diuretics, and intravenous barbiturates. Corticosteroids should be avoided.
- Randomised controlled trials do not support routine early **surgery** for spontaneous supratentorial non-aneurysmal ICH. However, if the patient deteriorates with a lobar haemorrhage, surgery may be discussed, and as for cerebellar infarcts surgery may be beneficial.

Haemostatic therapy

- **Recombinant activated factor VII** encourages coagulation at the site of vessel rupture, but may also induce thrombosis and has not been shown to be beneficial in randomised controlled trials.
- **In patients on oral anticoagulation** the outcome after ICH is worse; the INR should be normalised by prothrombin complex (PCC), fresh frozen plasma or vitamin K, but there are no randomised trials comparing these options. UK guidelines suggest PCC 30 U/kg.

SECONDARY PREVENTION TO REDUCE THE RISK OF NEW VASCULAR EVENTS

Secondary prevention consists of three complementary strategies (fig 5):

- optimal management of risk factors for stroke (all types of strokes and TIA)
- antithrombotic therapy (ischaemic stroke and TIA only)
- removal of the cause (all types of strokes and TIA).

Management of vascular risk factors

- **Blood pressure**: the blood pressure should be lowered even when ''normal'' at baseline, preferably with a diuretic, an ACE inhibitor or both, but probably not below about 130/70 mm Hg and with great care if there is bilateral severe carotid stenosis or occlusion (table 1).
- **Lipids**: randomised trials of statins show a 17% relative reduction in stroke risk: simvastatin (40 mg/day) or atorvastatine (80 mg/day) are safe, despite a small increase in the incidence of ICH and a very small risk of rhabdomyolysis (table 1). A statin should be given to all ischaemic stroke/TIA patients with an LDL-cholesterol above 1.00 g/l.
- **Smoking cessation** should halve the risk of mortality due to ischaemic heart disease within a year, and the risk of stroke should decline substantially within 2–5 years, according to observational studies.
- **Diabetes** There is no trial evidence that treatment reduces the risk of stroke but there is clear benefit on other target organs.
- **Oestrogens** are *not* recommended after a stroke or TIA, and any hormone replacement therapy should be stopped if possible.

Antithrombotic therapy

Antiplatelet agents in patients without a cardiac source of emboli

Antiplatelet drugs provide an absolute reduction of serious vascular events (myocardial infarction, stroke, vascular death) of about 1–2%/year in patients with TIA or ischaemic stroke.

- **Aspirin** is effective between 75 and 1300 mg per day. Its safety profile is better at lower doses (75–150 mg/day).
- **Clopidogrel** (75 mg/day) is perhaps slightly more effective than aspirin and has a good safety profile. It is the first choice in patients with aspirin intolerance, but its use is limited by its cost.
- **The combination of modified release dipyridamole (200 mg twice daily) with aspirin (at least 50 mg daily)** after a TIA or a minor ischaemic stroke is more effective than aspirin alone.
- **The combination of clopidogrel with aspirin** reduces the risk of ischaemic events

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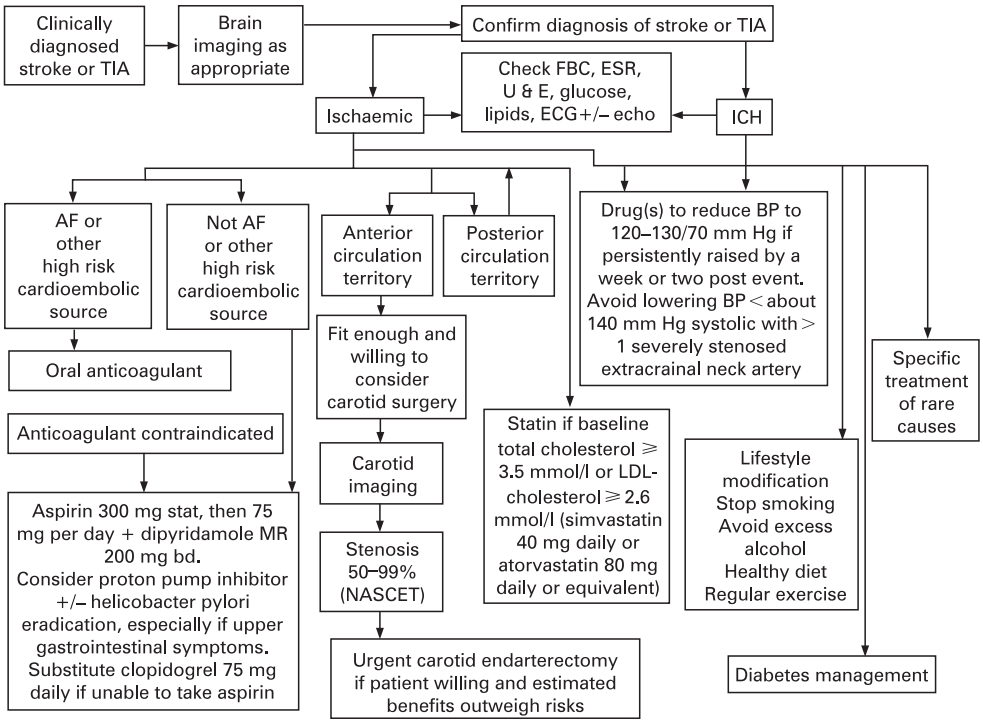

Figure 5 Strategy for secondary stroke prevention. (Reproduced with permission from *Stroke: practical management*. Blackwell Science, 2008.)

but is counterbalanced by an increased risk of bleeding.

In practice, aspirin (50–325 mg/day), clopidogrel (75 mg/day) and modified release dipyridamole (200 mg twice daily) with aspirin (50–75 mg daily) are the three antiplatelet regimens of choice for patients in sinus rhythm. The exact choice is guided by the safety profile, tolerance, associated disorders and cost. The combination of aspirin with clopidogrel should not be given, except for patients with recent coronary stenting or an acute coronary syndrome.

Antiplatelet agents—and oral anticoagulants—in patients with a cardiac source of emboli

Oral anticoagulation is better than aspirin for secondary prevention in patients with atrial fibrillation and should, therefore be preferred if possible. When it is not possible, aspirin should be used.

- **In patients with TIA or minor ischaemic stroke and atrial fibrillation**, oral anticoagulation (warfarin, target INR 2–3) reduces the absolute risk of stroke by 8% per year (from 12% to 4%).
- **In patients with mechanical valvular prosthesis** the target INR is 3–4.
- **Warfarin is sometimes given** for the antiphospholipid syndrome, paradoxical embolism, cervical-artery dissection and intracranial dolichoectasia, but these strategies are not supported by randomised trials.

Removal of the cause

Carotid surgery

The two major predictors of risk of ipsilateral ischaemic stroke in patients with internal carotid artery stenosis are recent relevant cerebrovascular symptoms (that is, ipsilateral to the stenosis) and the degree of stenosis (table 2).

- On average, surgery provides extra benefit over and above best medical therapy, irrespective of gender and type of qualifying event (cerebral or ocular) for symptomatic stenosis of 70% or more.
- There is some benefit of surgery for 50–70% stenosis, except in women and those with ocular events.
- There is no benefit of surgery for stenosis <50%.

Table 1 Secondary prevention after stroke with risk factor management

Treatment	Relative risk reduction in stroke	Absolute risk reduction in stroke in 1 year	Number-needed-to-treat to prevent one stroke in one year
Antihypertensive therapy	23%	1.4%	71
Statins	17%	1.5%	67

Blood pressure and cholesterol lowering will have an additional benefit in reducing coronary events.

Table 2 Secondary prevention of stroke with carotid surgery

Severity of stenosis	Relative risk reduction	Absolute risk reduction	Number-needed-to-operate to prevent one stroke in 2 years
Symptomatic (70–99%)	65%	13%	8
Symptomatic (50–69%)	30%	7%	14
Symptomatic (<50%)	No benefit	No benefit	No benefit

- The benefit of surgery is modest in patients with ocular events, lacunar infarcts, contralateral carotid occlusion, and with collapse of the vessel distal to very severe stenosis.
- The benefit of surgery is greatest within days of the relevant cerebrovascular event and declines rapidly over time, so that it is minimal after 3–6 months.
- There is little benefit for surgery in patients with asymptomatic carotid stenosis

Carotid angioplasty/stenting

Despite the theoretical advantages, and the lack of a neck incision, there is as yet no randomised trial evidence that carotid stenting/angioplasty is as safe as carotid surgery in the short term, or reduces the risk of stroke as effectively in the long term.

Surgical, radiosurgical and interventional radiological treatment of intracranial vascular malformations

Treatment options depend mainly on the nature, size and location of the malformations, there are no randomised trials, and decisions have to be individualised.

CONCLUSIONS

- The incidence of stroke is now higher than that of acute coronary syndromes.
- Stroke is characterised by a sudden or rapidly developing loss of cerebral function without any cause other than vascular, and includes both infarcts and haemorrhages.
- Intracerebral haemorrhage accounts for about 10% of all strokes in white populations, and cerebral ischaemia for 90%. Brain imaging is mandatory to differentiate between these two main pathological types of stroke.
- TIAs last only a few minutes in most cases and are markers of a high risk of ischaemic stroke, especially over the following few days.
- In white populations, the most frequent causes of cerebral ischaemia are large-artery atherosclerosis, atrial fibrillation, and intracranial small vessel disease.
- The main causes of intracerebral haemorrhage are structural abnormalities of blood vessels due to chronic arterial hypertension, cerebral amyloid angiopathy and vascular malformations.
- Besides non-modifiable risk factors (increasing age, male gender, and familial predisposition), several risk factors can be treated to prevent stroke, especially high blood pressure, high blood cholesterol, and cigarette smoking.
- In all types of stroke (ischaemic and haemorrhagic) the short-term risks are early epileptic seizures, delirium, raised intracranial pressure, and non-specific complications such as pressure sores, pneumonia, and pulmonary embolism. The long-term risks are dementia, depression, late epileptic seizures, and physical disability.
- Stroke unit care reduces case fatality and handicap in all types of strokes. In ischaemic strokes rt-PA within three hours is the standard therapy, or aspirin 300 mg when thrombolysis is not appropriate.
- In ischaemic strokes, the risk of early (and later) recurrence declines with time and depends on the cause. New ischaemic events in other vascular territories are also frequent.
- To reduce the risk of any new vascular events after a stroke or TIA, the three complementary strategies are: optimal management of risk factors for stroke (for all types of strokes and TIA), antithrombotic therapy (for ischaemic stroke and TIA only), and carotid surgery for severe symptomatic carotid stenosis.

Competing interests: None declared.

Further reading

- Warlow C, van Gijn J, Dennis M, *et al*. *Stroke: practical management*. Third edition Blackwell Science, 2008.
- Antithrombotic_Trialists'_Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;**324**:71–86.
- Bamford J, Sandercock P, Dennis M, *et al*. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet* 1991;**337**:1521–6.
- Hacke W, Donnan G, Fieschi C, *et al*. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet* 2004;**363**:768–74.
- Hankey GJ, Warlow CP. Treatment and secondary prevention of stroke: evidence, costs, and effects on individuals and populations. *Lancet* 1999;**354**:1457–63.
- Rothwell PM, Coull AJ, Silver LE, *et al*. Population-based study of event-rate, incidence, case fatality, and mortality for all acute vascular events in all arterial territories (Oxford Vascular Study). *Lancet* 2005;**366**:1773–83.
- Rothwell PM, Eliasziw M, Gutnikov SA, *et al*. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet* 2004;**363**:915–24.
- Rothwell PM, Giles MF, Flossmann E, *et al*. A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack. *Lancet* 2005;**366**:29–36.
- Warach S, Dashe JF, Edelman RR. Clinical outcome in ischemic stroke predicted by early diffusion-weighted and perfusion magnetic resonance imaging: a preliminary analysis. *J Cereb Blood Flow Metab* 1996;**16**:53–9.
- Weimar C, Kraywinkel K, Rodl J, *et al*. Etiology, duration, and prognosis of transient ischemic attacks: an analysis from the German Stroke Data Bank. *Arch Neurol* 2002;**59**:1584–8.

2008;**8**:263–272. doi:10.1136/jnnp.2008.149401