Time is of the essence when treating stroke. Therefore, patients should be transferred immediately to a hyperacute stroke unit for management, which will depend on the type and severity of the stroke.

**Stroke**

acute management

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The most important factor in the treatment of stroke is time — early management is vital for optimising patient outcomes and reducing disability caused by stroke. Following initial assessment, patients who are likely to have suffered from a stroke recently should be referred immediately to a hyperacute stroke unit (see Box 1) for rapid investigation and multidisciplinary management, including early rehabilitation and frequent monitoring.

Specific treatment for stroke depends on the underlying pathology (ischaemic versus haemorrhagic), cause (eg, artery stenosis, cardiac embolism or venous thrombosis) and site of the stroke.

**Ischaemic stroke**

**Intravenous thrombolysis** Intravenous thrombolysis with the recombinant human tissue plasminogen activator alteplase (rt-PA) within 4.5 hours of onset of ischaemic stroke can significantly improve patient outcomes. Although other thrombolytic drugs have been investigated for the treatment of ischaemic stroke, alteplase has the largest body of clinical evidence to support its use and, currently, is the only medicine licensed for this indication.

Alteplase has a short half-life of approximately five minutes and is administered as an initial IV bolus (10% of the total dose) followed by the remaining 90%, which is infused over 60 minutes. The dose is calculated using patient weight (0.9mg/kg) up to a maximum of 90mg. This dose is different from that used for thrombolysis in myocardial infarction or pulmonary embolism.

There are strict exclusion criteria for thrombolysis to ensure that it is not given to patients with a high risk of serious bleeding or where the risk of haemorrhage outweighs the benefits of thrombolysis (outlined in the summary of product characteristics for alteplase).

Alteplase should only be administered within a well organised stroke unit that has immediate access to the required facilities (eg, imaging equipment) and staff trained in interpreting images, delivering thrombolytic therapy and monitoring for complications. Protocols should be available for the management of thrombolysis.

The phrase “time is brain” is commonly used to highlight the point that outcomes are improved when treatment is started quickly. Treatment is twice as effective if it is administered within 1.5 hours of the onset of stroke symptoms compared with treatment in the 1.5–3 hour window. The outcomes of treatment are poorer still when alteplase is administered after three hours. Despite this, a modest improvement in clinical outcomes can occur when alteplase is given up to 4.5 hours after symptom onset. Thrombolysis in this later time window is associated with more symptomatic intracranial haemorrhage, but can be given based on clinical judgement. The third international stroke trial (IST-3) is currently investigating thrombolysis with alteplase for patients up to six hours after the onset of stroke symptoms.

The 2010 “National sentinel stroke audit”, which assessed stroke services in England, Wales and Northern Ireland, showed that 5% of stroke patients had received thrombolysis although 14% had been eligible (based on criteria from the National Institute for Health and Clinical Excellence). Nevertheless, it also showed that the rate of thrombolysis had increased from 1.8% in 2008, mostly due to investment in hyperacute stroke services that operate 24 hours a day, seven days a week.

**Mechanical clot retrieval** Mechanical clot retrieval by experienced interventional neuroradiologists can be considered for patients unsuitable for thrombolysis.

Research has shown that mechanical clot retrieval with the MERCI (mechanical embolus removal in cerebral ischaemia) device within eight hours of stroke onset is associated with higher rates of restored blood flow (ie, recanalisation) than historical controls.

**Box 1: Hyperacute stroke units**

In the UK, hyperacute stroke units have been established to ensure access to early diagnosis and management of stroke. Such units deliver high-dependency multidisciplinary care, including 24-hour access to expert clinical assessment, timely brain imaging, opinion of a specialist stroke consultant and administration of intravenous thrombolysis to patients who can benefit from this treatment.
Antiplatelet medicines All patients with an acute ischaemic stroke, including those with atrial fibrillation, should be prescribed aspirin 300mg daily as soon as possible after the onset of symptoms. Ideally, this should be given orally but if the patient is dysphagic administration using an enteral feeding tube or via the rectal route may be more appropriate.

If a patient has received thrombolysis, antiplatelet therapy should not be started until 24 hours have passed and repeat imaging has ruled out haemorrhagic transformation of the infarct.

Aspirin treatment should be continued for up to 14 days, or until a plan for long-term secondary prevention with an antiplatelet medicine or an anticoagulant is decided (see accompanying article, p209).

**Statin therapy** Following an acute ischaemic stroke, patients who were already taking a statin should continue to do so. However, for patients who were not previously taking a statin, one should be started 48 hours after the onset of symptoms — starting a statin immediately is not recommended.

**Haemorrhagic stroke** Haemorrhagic stroke will sometimes require neurosurgical intervention, but is usually managed medically.

**Correcting coagulopathy** Patients with a coagulation factor deficiency or thrombocytopenia should receive appropriate factor replacement therapy or platelets, respectively.

Patients taking oral anticoagulants constitute 12–14% of patients who suffer haemorrhagic stroke. For patients with oral anticoagulant-associated haemorrhagic stroke and an international normalised ratio >1.4, the oral anticoagulant should be discontinued for at least 10–14 days and their INRs should be normalised using a combination of prothrombin complex concentrate and intravenous vitamin K as soon as possible.

Coagulation status should be monitored closely and a haematology review obtained in the acute phase. Prothrombin complex concentrates, such as Beriplex or Octaplex, will normalise clotting within minutes, and are generally preferred over glucose-containing preparations. There is no evidence that using plasma expanders (dextran, hydroxyethyl starch or albumin) has any benefit over standard fluid replacement.

**Blood pressure** Patients with high, low or greatly fluctuating blood pressure in the first 24 hours following an ischaemic stroke are more likely to have poorer outcomes. This is possibly due to cerebral hypoperfusion (caused by low blood pressure) and cerebral oedema or haematoma expansion (caused by high blood pressure). Despite this, evidence regarding optimal blood pressure strategies in the acute phase of stroke, and how these translate into patient outcomes, is lacking.

Potter and colleagues reported that lisinopril and labetalol use within 36 hours of stroke onset did not increase serious adverse events and reduced three-month mortality by half. However, the recent SCAST trial reported that candesartan use in acute stroke patients with hypertension did not improve vascular outcomes during the first six months, and may be associated with poorer functional outcomes. In the COSSACS trial, continuation of antihypertensive medication within 48 hours of acute stroke was not associated with improved outcome or increased adverse events.

Many patients have spontaneous declines in blood pressure over the first week after stroke, and active blood pressure management is not recommended routinely, except in hypertensive emergencies. Cautious blood pressure reduction of 15–25% in the first 24 hours of stroke onset may be considered if blood pressure exceeds 220/120mmHg in ischaemic stroke, or if systolic blood pressure exceeds 160mmHg for patients with...
haemorrhagic stroke. Hypertensive patients who are potential candidates for thrombolysis should have their blood pressure lowered to 110/75 mmHg before thrombolysis and kept below 105/70 mmHg for at least 24 hours after thrombolysis to reduce the risk of symptomatic haemorrhagic transformation.

If treatment is indicated, intravenous antihypertensive drugs with a short half-life should be used first line. In UK hyperacute stroke units, labetalol, glyceryl trinitrate and, occasionally, sodium nitroprusside are used. Sublingual nifedipine should not be used due to the risk of an abrupt decrease in blood pressure. Recommendations for the management of hypertension in the acute phase of stroke are summarised in Box 2 (p208).

Low blood pressure can usually be raised by adequate rehydration with saline infusions, but patients with low cardiac output occasionally require inotropic support.

Blood glucose Hyperglycaemia in the acute phase of stroke is common, even for non-diabetic patients, possibly as a stress response. It is associated with larger infarcts and poorer functional outcomes. Following thrombolysis, hyperglycaemia may also be associated with increased risk of haemorrhagic transformation of ischaemic stroke.

In the acute phase, patients’ blood glucose should be controlled tightly, aiming for a blood glucose concentration of 4–11 mmol/L. If required, this can be achieved using continuous infusions of insulin, the rates of which are adjusted based on patients’ blood glucose readings. These insulin infusions can be co-administered with an infusion of 5% glucose (given at a constant rate) to avoid hypoglycaemia. Avoiding glucose solutions for fluid replacement in the acute phase of stroke may also help to avoid high blood glucose levels.

Oxygen Theoretically, oxygen therapy could potentially reverse hypoxia in acute ischaemic stroke through increased cerebral oxygenation and reduced cerebral oedema. However, high doses of oxygen could also be harmful by increasing oxidative stress through increased oxygen free-radical production.

In a quasi-randomised study of oxygen therapy in non-hypoxic acute stroke patients, 100% normobaric oxygen at 3 L/min for 24 hours via nasal catheter did not improve patient outcomes but increased mortality among patients with minor or moderate stroke.

Oxygen therapy (2–6 L/min via nasal cannulae) should only be considered in acute stroke patients if oxygen saturation falls below 95% (or below 92% according to American guidelines). The British Thoracic Society recommends using targeted oxygen therapy in all acutely ill patients. The usual target oxygen saturation of 94–98% is appropriate for most patients, but a target of 88–92% should be used for patients at risk of hypercapnic respiratory failure, for example those with chronic obstructive pulmonary disease. The ongoing “Stroke oxygen study” is investigating fixed-dose supplemental oxygen in the first 72 hours post-stroke.

There is no good evidence that hyperbaric oxygen improves clinical outcomes for patients with acute stroke; it should not be used outside of clinical trials.

Temperature Increased body temperature in the acute phase of stroke is associated with poor outcome and the cause of the elevated temperature should be investigated and treated where appropriate. Although no evidence exists that either physical cooling or the use of antipyretic medicines to lower body temperature affects outcomes, it is common practice to treat raised body temperature (>37.5°C) with paracetamol.

Venous thromboembolism prevention In the acute phase following a stroke, patients are at increased risk of venous thromboembolism (VTE). Early hydration and early mobilisation can reduce the risk of VTE. Anti-embolism stockings should not be used for stroke patients because they have been shown to increase adverse events without reducing rates of VTE.

Pharmacological thromboprophylaxis is not recommended routinely for acute stroke patients since the benefit of VTE reduction is offset by an increased risk of bleeding. However, some patients have a particularly high risk of VTE and larger trials are needed to study the use of low-dose heparin for such patients. For patients in whom the risk of VTE outweighs the risk of haemorrhagic transformation, prophylactic doses of low molecular weight heparins should be considered in preference to unfractionated heparin, except in renal failure, and reviewed regularly.

For patients who have a high risk of VTE and who have suffered a haemorrhagic stroke, or who are at high risk of bleeding, the use of foot impulse or intermittent pneumatic compression devices should be considered.

References
Box 2: Hypertension management for patients in the acute phase following stroke

<table>
<thead>
<tr>
<th>TYPE OF STROKE</th>
<th>GUIDELINES</th>
<th>RECOMMENDATIONS</th>
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<tbody>
<tr>
<td>Ischaemic</td>
<td>National Institute for Health and Clinical Excellence</td>
<td>Antihypertensive treatment is recommended only in a hypertensive emergency with hypertensive encephalopathy, hypertensive nephropathy, hypertensive cardiac failure or myocardial infarction, aortic dissection or pre-eclampsia/eclampsia. Consider blood pressure (BP) reduction to ≤185/110mmHg for people who are candidates for thrombolysis.</td>
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<tr>
<td>Scottish Intercollegiate Guidelines Network</td>
<td>Routinely, BP should not be actively managed for patients in the acute phase of ischaemic stroke.</td>
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<tr>
<td>European Stroke Organisation</td>
<td>Before thrombolysis it is recommended to reduce BP to &lt;185/110mmHg; abrupt lowering of BP should be avoided.</td>
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<tr>
<td>American Heart Association/American Stroke Association</td>
<td>Antihypertensive therapy may be considered if systolic BP &gt;220mmHg or diastolic BP &gt;120mmHg; BP should be reduced cautiously — by 15–25% within the first day.</td>
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<tr>
<td>For patients eligible for thrombolysis or other acute reperfusion intervention, antihypertensive therapy is recommended if systolic BP &gt;185mmHg or diastolic BP &gt;110mmHg. Maintain BP ≤180/105mmHg during and for 24 hours after thrombolysis or other acute reperfusion intervention.</td>
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Haemorrhagic

| National Institute for Health and Clinical Excellence | Anti-hypertensive treatment is recommended if systolic BP >200mmHg. |
| European Stroke Initiative | In patients with known prior hypertension or signs of chronic hypertension, maintain BP ≤160/105mmHg; if treatment is necessary, a target BP of 160/100mmHg (or a mean arterial pressure (MAP) of 120mmHg) is recommended. |
| For patients without known hypertension, maintain BP ≤160/95mmHg. If treatment is necessary, a target BP of 150/90mmHg (or MAP of 100mmHg) is recommended. These limits and targets should be increased in patients with increased intracranial pressure (ICP) to ensure sufficient cerebral perfusion pressure of at least 60–70mmHg. |
| Immediate antihypertensive therapy may also be appropriate for patients with concomitant acute myocardial ischaemia, cardiac insufficiency, acute renal failure, acute hypertensive encephalopathy or aortic arch dissection. Rapid and excessive lowering of BP should be avoided. |

American Heart Association/American Stroke Association

| If systolic BP >220mmHg or MAP >150mmHg consider aggressive BP reduction, with continuous intravenous infusion of antihypertensive. If there is the possibility of elevated ICP, consider monitoring ICP and reducing BP if systolic BP >180mmHg or MAP >130mmHg using intermittent or continuous intravenous antihypertensives, and maintain a cerebral perfusion pressure ≥80mmHg. |
| Where there is no evidence of elevated ICP and systolic BP >160mmHg or MAP >130mmHg, consider modest BP reduction (eg, target MAP 110mmHg or target BP 160/90mmHg) using intermittent or continuous intravenous antihypertensives. |

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