Management of stroke
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This article outlines the current evidenced based practice for stroke care. It outlines many of the recommendations in the National Clinical Guidelines for Stroke published by the Royal College of Physicians. It also covers all aspects of multidisciplinary stroke care from initial assessment and acute treatment to rehabilitation strategies and management of complications. The article concludes with an examination of the latest evidence for secondary prevention of cerebrovascular disease.

The profile of stroke care in the UK is increasing with several factors contributing to the change. Firstly, in March 2000, the Royal College of Physicians published its National Clinical Guidelines for Stroke. The stimulus for the guidelines came from evidence provided by National Sentinel Audit of Stroke and a Clinical Standards Advisory Group report, confirming suboptimal stroke care.

The second contributing factor is renewed government awareness of the importance of stroke given that stroke is the third highest cause of death in the UK, is the biggest single cause of major disability, and uses 4% of the total annual NHS expenditure. The first government initiative came in 1999, when the Department of Health published Saving Lives: Our Healthier Nation. The government made reduction in death from coronary heart disease and stroke in people aged less than 75 years one of the four priority areas built up particularly over the last decade, which informs all aspects of stroke care from acute treatment to long term rehabilitation.

ROYAL COLLEGE OF PHYSICIANS' GUIDELINES
Many of the recommendations made in this article are derived from the National Clinical Guidelines for Stroke published by the Royal College of Physicians (London) in March 2000 and updated in February 2002. The guidelines cover the management of patients with acute stroke from onset, through rehabilitation, to the longer term. They are evidence based and each recommendation is accompanied by both a level of evidence (Ia–IV) and grade of recommendation (A–C); see table 1.

They are available in book format from the Royal College of Physicians and can be downloaded from the college’s home page at http://www.rcplondon.ac.uk. The Scottish Intercollegiate Guidelines Network has also published guidelines on specific aspects of stroke care and these are currently being updated with the expectation that they will be available within the next 12 months on http://www.sign.ac.uk.

DIAGNOSIS
The World Health Organisation (WHO) definition (1978) defines stroke as a clinical syndrome typified by rapidly developing signs of focal or global disturbance of cerebral functions, lasting more than 24 hours or leading to death, with no apparent causes other than of vascular origin. A senior clinician should review all patients admitted with presumed stroke to clinically confirm diagnosis (B). Care is needed in younger stroke patients (age <45) or if there is any unusual feature such as unexplained fever, severe headache, or gradual progression of signs. The consensus guidelines and the National Service Framework state that brain imaging should be undertaken within 48 hours of stroke; however, imaging should be undertaken urgently in the following situations—depressed level of consciousness, fluctuating symptoms, papilloedema, neck stiffness, fever, severe headache, previous trauma, anticoagulant treatment, or bleeding diathesis (B).

HOW SHOULD CARE BE DELIVERED?
Trials of stroke units have compared conventional care with a variety of services labelled as “stroke units”. There are, however, certain features that all these services have in common. The stroke service should be centred in a hospital based stroke unit. It should be staffed by a multidisciplinary team with expertise in stroke care and rehabilitation (A). The team should work to agreed protocols for common problems (A) and provide educational programmes for staff, patients, and carers (A). The Royal College of Physicians’ guidelines strongly recommended that the WHO’s international classification of impairments, disabilities, and handicaps terminology be used.

Abbreviations: CI, confidence interval; OR, odds ratio; r-PA, recombinant tissue plasminogen activator; TIA, transient ischaemia attack; WHO, World Health Organisation

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WHERE SHOULD CARE BE DELIVERED?
All patients with stroke should be admitted to hospital (A) unless they present late and have few or no residual symptoms. The evidence for organised inpatient (stroke unit) stroke care is robust and the Stroke Unit Trialists’ Collaboration showed that compared with alternatives, stroke unit care showed reductions in the odds of death recorded at follow up (odds ratio (OR) 0.86; 95% confidence interval (CI) 0.71 to 0.94; p=0.005). The odds of death or institutionalisation care and death or dependencies were also significantly reduced. Outcomes were independent of patient age, sex, and stroke severity and appeared to be better in stroke units based in a geographically discrete ward. There was no indication that organised stroke unit care resulted in increased hospital stay and it is likely to be cost saving. Stroke units have also been shown to be superior to other forms of organised stroke care. In a study where patients were randomly assigned to stroke unit care, general wards with stroke team support, or domiciliary stroke care, mortality and institutionalisation rates at one year were lower in patients who received care on the stroke ward. The benefits of stroke unit care have been shown to persist at 10 years after initial stroke.

Early supported discharge from hospital to a specialist rehabilitation team providing care in the patient’s own home has been shown to be feasible for selected patients, with clinical outcomes at one year similar for the early discharge group and those who remained in hospital (A). Well designed controlled study but without randomisation or well designed quasiexperimental study or well designed descriptive study. The guidelines state that specialist stroke services can be delivered to patients after the acute phase, equally effectively in hospital or in the community provided that the patient can transfer from bed to chair before going home and that they continue to be seen by a specialised multidisciplinary stroke team (A).

There is currently no evidence from clinical trials to support a radical shift in the care of acute stroke patients from hospital based care. Patients should only be managed at home if acute assessment guidelines can be adhered to and the services organised for home are flexible, and part of a specialist stroke service (A). The guidelines do allow for the management of some patients in the community, particularly those with transient ischaemia attacks (TIAs) and strokes with good recovery. The consensus was that these patients could be managed at home provided they had access to a neurovascular clinic within two weeks (C). More than one TIA within a short period (crescendo TIA) requires admission to hospital (C). The guidelines are not prescriptive in defining a short period but the authors consider that recurrent TIAs within one week merit admission.

### Table 1: Type of evidence and grade of recommendation from Royal College of Physicians’ guidelines

<table>
<thead>
<tr>
<th>Type of evidence</th>
<th>Grade of recommendation</th>
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<tbody>
<tr>
<td>Meta-analyses of randomised controlled trials or at least one RCT</td>
<td>A</td>
</tr>
<tr>
<td>Well designed controlled study but without randomisation or well designed quasiexperimental study or well designed descriptive study</td>
<td>B</td>
</tr>
<tr>
<td>Expert committee reports, opinions and/or experience of respected authorities</td>
<td>C</td>
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RCT, randomised controlled trial.

ACUTE INTERVENTION
A large number of trials have been conducted on the use of pharmacological agents in the acute phase of stroke. Few have yielded positive results despite promising data from animal models. There is insufficient evidence to support the use of any neuroprotective agents, prostacyclin analogues or methylxanthines (vasodilators), steroids, or osmotic diuretics to reduce oedema.

Patients with acute ischaemic stroke should receive aspirin (160–300 mg) as soon as possible after stroke if a diagnosis of haemorrhage is considered unlikely (A). Ideally brain imaging to rule out haemorrhage should be performed before starting aspirin. This evidence comes from two large randomised controlled trials, the International Stroke Trial (IST) and Chinese Acute Stroke Trial (CAST) involving a total of 40 000 patients. Combining data from both trials gives a significant increase in independence at six months (OR 0.94; 95% CI 0.91 to 0.98), which in absolute terms translates to 13 more patients who were alive and independent at six months for every 1000 patients treated. The increase in symptomatic intracranial haemorrhages (two per 1000 patients) is offset by the reduction in recurrences (seven per 1000 patients treated) (A).

Perhaps the most exciting acute pharmacological intervention is thrombolysis. It is associated with an increase in symptomatic intracranial haemorrhages but disability is reduced in survivors. A meta-analyses of thrombolysis in acute stroke reveals that for every 1000 patients treated with thrombolysis, 44 avoided death or dependency. The most promising agent is recombinant tissue plasminogen activator (rt-PA) administered intravenously within three hours of symptom onset compared with placebo, patients treated with rt-PA were at least 30% more likely to have minimal or no disability at three months (A). However, some authors have challenged conclusions drawn from the NINDS Stroke Study Group and questioned the wisdom of expanding thrombolysis programme based on the results of one relatively small trial. Information on thrombolysis is based on only 5000 patients and further knowledge on patient selection in terms of stroke severity, stroke subtype, concomitant use of antithrombotic drugs, and computed tomogram appearance is still needed. A measured approach is reflected in the Royal College of Physicians’ guidelines, which state that use of thrombolysis should be restricted to a specialist centre with appropriate experience.

CARERS AND FAMILIES
Patients and carers want to be looked after by knowledgeable staff, who understand the full range of their needs after a stroke. Unfortunately the diagnosis and management plan are not always explained in a manner that all patients and carers can comprehend and recall. The guidelines recommend that families are involved in the decision making process and have input into future plans for the patient (C). A separate version of the National Clinical Guidelines, available through the Stroke Association, has been produced for patients and their carers setting out the standards that a patient should expect to receive during the course of their illness.

Caring for a stroke patient can be very difficult and emotional distress is seen in 53% of caregivers at six months after stroke. Caregivers are more likely to be depressed if the patients are severely dependent or emotionally distressed themselves. The stroke team must be alert to recognising carer stress and helping carers in this difficult situation (B). Disseminating information about the nature of stroke and on relevant local and national services improves patient and carer knowledge (A). The introduction of stroke family support workers has been shown to significantly increase social activities and quality of life for carers and to improve patients’ and carers’ satisfaction in terms of communication and support. Family support workers have not been shown to improve patient outcomes in term of disability, handicap, and quality of life.
If the use of thrombolysis does become widely accepted in the UK there will need to be a dramatic change in the organisation of stroke services, such that they are able to deliver patients to specialist units capable of giving the drug within three hours of the onset of symptoms, having already had brain imaging and detailed clinical assessment. While thrombolysis is only ever likely to be given to a small proportion of stroke sufferers the improvements in acute stroke care that result from establishing services that are capable of giving the drug will, in the view of the authors, result in reductions in mortality and morbidity in the stroke population as a whole. Immediate anticoagulant therapy in patients with acute ischaemic stroke is not associated with net short or long term benefit. Although acute anticoagulant therapy is associated with about nine fewer recurrent ischaemic strokes and four fewer pulmonary emboli per 1000 patients treated, the benefit is offset with a similar sized nine per 1000 increase in symptomatic intracranial haemorrhages. While there is evidence for the secondary prevention of ischaemic stroke by anticoagulating patients in atrial fibrillation, immediate anticoagulation of patients with ischaemic stroke and atrial fibrillation is not beneficial. The Royal College of Physicians’ consensus guidelines recommend that anticoagulation should not be started until 14 days after the acute event (A).

There is evidence for acute anticoagulation in the specific stroke syndrome of cerebral venous thrombosis but insufficient evidence to advise on the use of anticoagulants in other subgroups of patients such as those with vertebral occlusion or large vessel dissection. It is unlikely that such evidence will ever be sufficient, given the rarity of the conditions. The practice of the authors is currently to anticoagulate patients with dissection and those with progressive ischaemic lesions in the posterior circulation. There have been few trials of the effect of careful maintenance of normal physiology in the acute phase of stroke. The evidence for acute lowering of blood pressure, body temperature, or administration of hyperosmolar agents such as mannitol and glycerol to reduce brain oedema is not robust enough for recommendation. However, the guidelines state it is important to keep physiological variables such as hydration, temperature, nutrition, and oxygenation within normal range in the acute phase of stroke (C). This may be achieved in an acute stroke unit. Such units are still uncommon in the UK but are well developed elsewhere in Europe. This difference may explain the comparatively better survival and impairment outcomes seen in some European centres.

REHABILITATION

There is no evidence to support selection criteria for more active rehabilitation or admission to a stroke unit. If anything, those with more severe stroke have the most to gain from admission. The first step in the rehabilitation of the stroke patient begins with assessment of disability. Assessment is effective in rehabilitation when, as happens in a stroke unit, it is linked to later management (A). The guidelines recommend that assessments and measures with proved reliability and validity are used and that patients are assessed at appropriate intervals (C). In practical terms this requires prompt assessment of the patient’s consciousness level, swallowing, nutritional status, cognition and mobility and ongoing need on the stroke unit.

Dysphagia occurs in about 45% of all stroke patients admitted to hospital. It is associated with more severe strokes and with a worse outcome. Dysphagia management involving an initial swallow screen, diet modification, and compensatory swallowing techniques reduces the risk of aspiration pneumonia. Patient and family instruction in the management of dysphagia has been shown to be as effective as daily therapist input, although this needs to confirmed in a larger study.

Maltreatment is also common and is seen in 50% of patients one week after stroke. Routine oral or enteral protein supplement intake improves nutritional indices but there is no evidence that it affects outcome. In the dysphagic patient, enteral nutrition can be supplied by either nasogastric tube or percutaneous endoscopic gastrostomy. There is some evidence that percutaneous endoscopic gastrostomy feeding is superior to nasogastric feeding, but its insertion requires an invasive procedure. Questions concerning the most effective nutritional route as well as the timing of nutritional intervention after stroke are being addressed in a large randomised controlled trial, the FOOD trial. Information is available at http://www.dcn.ed.ac.uk/food.

Stroke can affect communication and speech in a variety of ways, including impaired motor speech production (dysarthria), impaired language skills (dysphasia), and impaired planning and execution of motor speech (articulatory dyspraxia). Deficits can be subtle and every patient with a communication difficulty needs to be assessed by a speech and language therapist. Speech therapy input is effective at improving communication, with short, intensive courses of speech therapy lasting 4–8 weeks proving most beneficial (B).

A physiotherapist with expertise in neurodisability should coordinate treatment to improve movement performance of patients with stroke (C). The effectiveness of motor and strength rehabilitation is being underpinned by new evidence and task specific strategies. Task specific training, such as reaching for coins, improves the reaching ability of the impaired limb more effectively than impairment focused approaches.

Resistance training significantly improved grip strength and the motor capacity of the impaired hand compared with traditional therapeutic strategies (Bobath) aimed at reducing enhanced muscle tone (B). Progressive resistive exercise studies have also been shown to improve gait, strength, activity, and mood. There is some evidence that increased intensity of therapist input improves outcome but some patients cannot tolerate intense therapist input. The guidelines recommend that patients receive as much as they find tolerable and at least working day (B). It is vital that patients have the opportunity to practise rehabilitation tasks.

The aim of rehabilitation is to regain patient independence and maximise ability in all activities of daily living. The need for special equipment such as a wheelchair or adapted cutlery should be assessed on an individual basis as review by an occupational therapist with specialist knowledge in neurological disability can significantly reduce disability and handicap (B). The provision of hoists or adaptation of the home environment may prevent the patient going to institutional care.

COMPLICATIONS

One of the challenges of stroke care and rehabilitation is the management of complications. Mood disorders are common after stroke and can be difficult to diagnose in the presence of speech disturbance. Crying after minimal provocation may be related to emotionalism. It can be diagnosed by a few simple questions and may be treated effectively with fluoxetine (A). A consensus statement from the guidelines recommends that patients should be screened for anxiety and depression within the first month after stroke and their mood kept under regular review (C). Patients diagnosed with a depressive disorder should be considered for antidepressive medication, even though the evidence for efficacy is very limited.

Pain after stroke varies in type, origin, and modes of treatment. Some pain is related to stroke damage and is termed
neuropathic or central pain. It has been shown to respond to tricyclic antidepressants (A). More often pain is mechanical arising from reduced mobility or an exacerbation of pre-existing osteoarthritis. Shoulder pain is seen in up to 30% of patients after stroke and is not as previously thought related to subluxation of the shoulder. Treatment should begin with simple analgesia and proper handling techniques. Previous evidence for shoulder strapping, steroid injection, or cutaneous electrical stimulation has not been confirmed in recent trials.

Spasticity is a motor disorder characterised by a velocity dependent increase in tonic stretch reflexes. It may lead to secondary complications such as muscle and joint contractures. In practice the management of spasticity requires several coordinated interventions including physiotherapy, drug treatment, and patient education. Physiotherapy using isokinetic strength training can improve strength and gait velocity without increasing spasticity, while drug therapy with either baclofen or tizanidine as an adjunct to physiotherapy has been shown to reduce spasticity. In patients with disabling or symptomatically distressing symptoms, botulinum toxin is safe and effective and can be targeted to individual muscles. The guidelines indicate that spasticity should be treated if causing symptoms, though functional benefit is uncertain (B).

Venous thrombolism is common after stroke and studies using radiolabelled fibrinogen leg scanning suggest that deep vein thrombosis occurs in up to 50% of patients with hemiplegia. The guidelines recommend that aspirin (75–300 mg daily) should be used (A) (in non-haemorrhagic strokes) and that compression stockings should be applied to patients with weak or paralysed legs (A). The final recommendation on the length of stocking to be used awaits results from the on-going CLOTs trial.

SECONDARY PREVENTION

People who have a stroke have a 30% chance of experiencing a recurrent stroke in the next five years. They are also at increased risk of myocardial infarction and other vascular events. Control of vascular risk factors is of paramount importance and strong evidence has emerged in recent years to guide our secondary prevention strategies. All patients should have their blood pressure checked and hypertension persisting for greater than one month should be treated (A). The treatment of hypertensive stroke survivors with blood pressure therapy decreases the recurrence of fatal and non-fatal stroke by 28% (95% CI 15 to 39). The target blood pressure is that recommended by the British Hypertension Society of an optimal blood pressure of systolic <140 mm Hg and diastolic <85 mm Hg.

A recent study on patients with a history of stroke or TIA looked at the benefit of treating patients with antihypertensive agents independent of baseline blood pressure. Patients treated with the angiotensin converting enzyme inhibitor, perindopril and a thiazide diuretic, indapamide, had a reduction in blood pressure of 12/5 mm Hg and reduced stroke risk by 43%. There were similar reductions in the risk of stroke in hypertensive and non-hypertensive groups. Further evidence of the efficacy of angiotensin converting enzyme inhibitors comes from the Heart Outcomes Prevention Evaluation (HOPE) study. Ramipril achieved a 32% relative risk reduction in primary and secondary stroke prevention in 9297 high risk patients. Baseline blood pressure was low at 139/79 mm Hg, while reduction in blood pressure seen was only 3.8 mm Hg systolic and 2.8 mm Hg diastolic. The efficacy of angiotensin converting enzyme inhibitors may be explained by their anti-inflammatory properties which lead to plaque stabilisation.

Patients with a previous ischaemic stroke should be started on an antiplatelet agent, aspirin (75–325 mg) daily, clopidogrel 75 mg daily, or a combination of low dose aspirin (75 mg daily) and dipyridimole modified release 200 mg twice a day (A). Where patients are intolerant of aspirin, treatment with clopidogrel or dipyridimole modified release should be instituted. In patients with prior TIA or stroke, antiplatelet therapy produced a 25% reduction in non-fatal stroke. There is no clear evidence for superiority of one antiplatelet agent over another or for combination antiplatelet therapy in cerebrovascular disease, but if a patient on one antiplatelet agent experiences a recurrent stroke then our practice is to add a second antiplatelet agent.

All patients with a history of stroke and atrial fibrillation should be considered for anticoagulation (A). Anticoagulant therapy decreases the odds of recurrent stroke in patients with atrial fibrillation by two thirds (OR 0.35; 95% CI 0.22 to 0.59). In those not suitable for anticoagulation, aspirin at a dose of 300 mg is a useful but less effective alternative.

The evidence for treatment of raised cholesterol comes from secondary prevention studies in patients with ischaemic heart disease. In patients with average cholesterol levels, after myocardial infarction, treatment with pravastatin led to a 27% reduction in stroke or TIA (95% CI 4% to 44%). The Royal College of Physicians’ guidelines recommend treatment with a statin in any individual with a history of ischaemic heart disease and a cholesterol >5.0 mmol (A), however this may be reviewed in the light of the recently published Heart Protection Study. In this study over 20 000 high risk vascular patients aged 40–80 years (including a cohort of 1820 patients with a history of non-disabling stroke or TIA) were randomised to simvastatin 40 mg daily or placebo for five years, independent of baseline cholesterol levels. Allocation to simvastatin produced a highly significant 25% (5%; 95% CI 15 to 34) proportional reduction in the incidence rate of first stroke. The benefits were seen across all age ranges and baseline cholesterol levels. A report outlining the influence of the intervention on recurrent events is being prepared.

Carotid ultrasound or magnetic resonance angiography should be considered for any patient with a carotid area stroke, minor or no residual disability, and in whom carotid endarterectomy may be appropriate. The benefits of an endarterectomy are seen in patients with a carotid artery stenosis greater than 70% (A). The operation should only be carried out by a specialist with a proved low complication rate (A).

SUMMARY

There have been major advances in recent years in the management of stroke both acutely and during rehabilitation. Secondary prevention that is effectively implemented is likely to significantly reduce the risk of stroke recurrence below levels currently seen. The National Service Framework for Older People will require a revolution in the organisation of stroke care in England, both in the hospital and the community. If this is to be achieved it will require investment. Stroke is in the process of being recognised as a subspecialty in the UK. If this leads to every district having a well trained team of stroke physicians the prospects for stroke care in the 21st century are bright.

QUESTIONS (ANSWERS AT END AFTER REFERENCES)

Q1. National stroke guidelines are published by?

Q2. What are the strengths of a stroke unit?

Q3. Most stroke patients can be managed in the community (true/false)

Q4. Who should be involved in making decisions concerning the patient?

A. The doctor only.
B. Anybody with an opinion.
C. Patient, carers/family members, and health care staff.
Q5. Anticoagulation should be given immediately after cerebral infarction, especially if considered likely to be cardioembolic (true/false)

Q6. Patients with severe stroke get the most benefit from a stroke unit (true/false)

Q7. Crying after stroke following minimum provocation is called?

Q8. Thrombolysis will have a more dramatic effect on stroke mortality than any intervention introduced so far (true/false)

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REFERENCES
ANSWERS

A2. Multidisciplinary teamwork with expertise in stroke care and rehabilitation.
A3. False. Patients should only be managed at home if acute assessment guidelines can be adhered to and that services provided are part of an organised stroke service.
A4. C.
A5. False. One should not start anticoagulation until 10–14 days after the cerebral infarct.
A6. True.
A7. Emotionalism.
A8. False. Stroke unit care is more powerful than any pharmacological agent.