SUBARACHNOID HAEMORRHAGE AND INTRACRANIAL ANEURYSMS: WHAT NEUROLOGISTS NEED TO KNOW

P J Kirkpatrick

J Neurol Neurosurg Psychiatry 2002;**73**(Suppl I):i28–i33

The incidence of stroke caused by subarachnoid haemorrhage (SAH) remains constant, with intracranial aneurysm rupture causing SAH in up to 5000 patients in the UK per annum. Although this represents less than 5% of all strokes, recognition is of crucial importance since intervention can radically alter outcome. The combined mortality and morbidity for aneurysm rupture reaches 50%; since the condition can affect individuals at any age, long term morbidity in survivors can be substantial.[1] Failure to diagnose SAH exposes a patient to the fatal effects of a further bleed, and also to complications which can now be avoided or successfully treated.[2 3]

PATHOLOGY

SAH refers to a leakage of blood into the subarachnoid spaces (fig 1A) which is a continuous space between the supratentorial and infratentorial compartments. A greater concentration of blood products around the site of the bleed is usual, but SAH originating from a focal source can be more diffuse and spread throughout wider aspects of the subarachnoid space. Haemorrhage can extend into adjacent parenchymal structures (fig 1B) and ventricular system, with associated high morbidity and mortality (fig 1C).

Inflammatory processes (table 1), excited by the presence of red cell breakdown products, affect the large vessels of the circle of Willis and smaller vessels within the subpial space.[4] These processes are complex, but combine to impair the adequate distribution of blood to affected territories. Cerebral ischaemia, often delayed by several days, is a common occurrence and major source of cerebral injury (fig 2).

Multiple sources for SAH are recognised (table 2), most arising from rupture of a vascular abnormality such as an intracranial aneurysm, cerebral arteriovenous malformations, or a dural fistula. The majority of the remainder are "angiogram negative" cases (10–20%), a possible consequence of peri-mesencephalic venous haemorrhage. The latter is of unknown aetiology but known to follow a benign clinical course with a very low tendency to rebleeding. Thus, no angiographic follow up is required for good clinical grade patients with SAH concentrated in the peri-mesencephalic cisterns who have a high quality normal angiogram.

The majority of vascular abnormalities causing SAH are aneurysms, and although a number of genetic conditions favouring aneurysm formation are known (table 3), environmental risk factors are more important with smoking, hypertension, and excess alcohol intake predominating.[5 6] Hormonal replacement therapy and the contraceptive pill are not risk factors.

INCIDENCE

The incidence of non-traumatic SAH varies between 8–12 per 100 000 per annum and increases with age, with children rarely affected. Regional variations have been described, but with equilibration of diagnostic tools across the world the incidence appears to be remarkably similar across cultures.[1 5]

CLINICAL PRESENTATION

SAH is an acute event, and usually associated with a dramatic and rapid onset of symptoms. A severe and explosive headache occurring without warning is typical and represents SAH until proven otherwise. With increasing severity of bleed, the clinical presentation is dominated by greater degrees of coma. Grading systems aid communication of SAH severity, the most popular of which is the World Federation of Neurosurgeons (WFNS) (table 4).[7] Focal symptoms and signs can be apparent, particularly when haemorrhage involves adjacent parenchyma in eloquent areas of the cortex. Occasionally, cranial nerve focal deficits occur (most commonly the oculomotor) and imply rupture adjacent to the affected nerve.

Meningeal irritation with neck symptoms occurs relatively late (after a few hours) and relies on migration of blood products onto the dural lining of the infratentorial compartment, an event

Correspondence to:
Mr PJ Kirkpatrick, Academic Neurosurgery Unit, Level 4, A Block, Box 167, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, UK; pjk21@medschl.cam.ac.uk

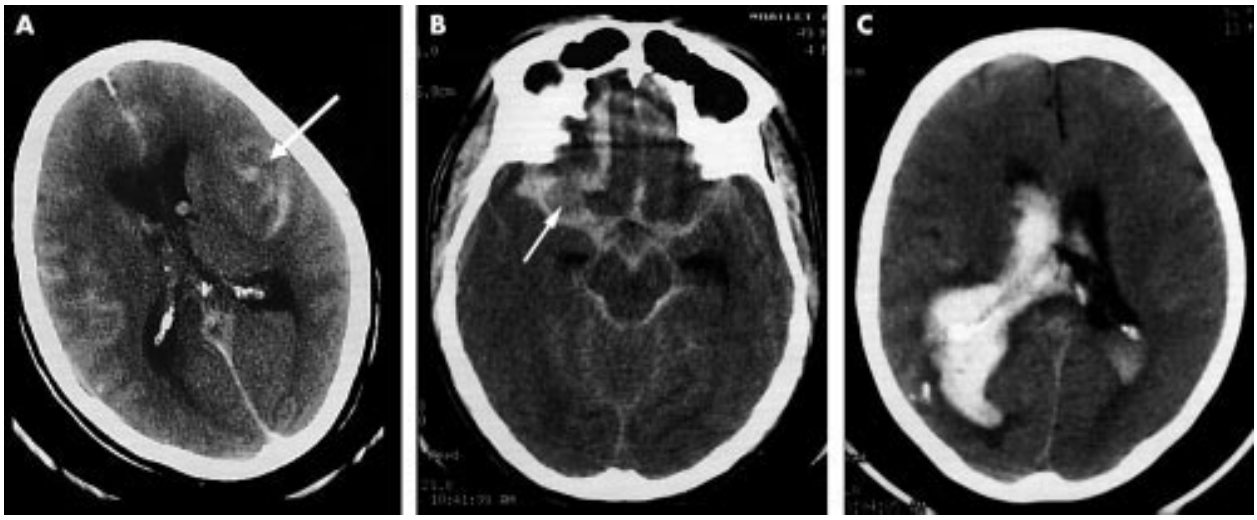

Figure 1 (A) Computed tomographic (CT) scan with diffuse subarachnoid blood maximum in the left Sylvian fissure (arrow). (B) CT scan showing collection of blood in the right Sylvian fissure. A giant aneurysm is seen in this location (arrow). (C) CT scan showing extensive intraventricular blood from rupture of anterior communicating aneurysm.

which should not be relied upon for diagnosis. Likewise optic nerve irritation, photophobia, and retinal haemorrhages occur late and can be absent. Subhyaloid haemorrhages (when present) are pathognomonic of SAH.

DIAGNOSIS

In all patients suspected of SAH, the first line investigation is a high resolution computed tomographic (CT) head scan (fig 1) which is 95% sensitive to the presence of SAH when undertaken within the first 24 hours of the ictus.[8] Thereafter the sensitivity reduces. The volume of blood seen on an early CT scan (graded according to Fisher, table 5)[9] attracts greater pathological consequences (tables 1 and 6, fig 1) and correlates with outcome. Head CT for suspected SAH is an emergency investigation, certainly undertaken within 6–12 hours of admission. Poor grade patients require immediate scanning once stabilised with aggressive resuscitation.

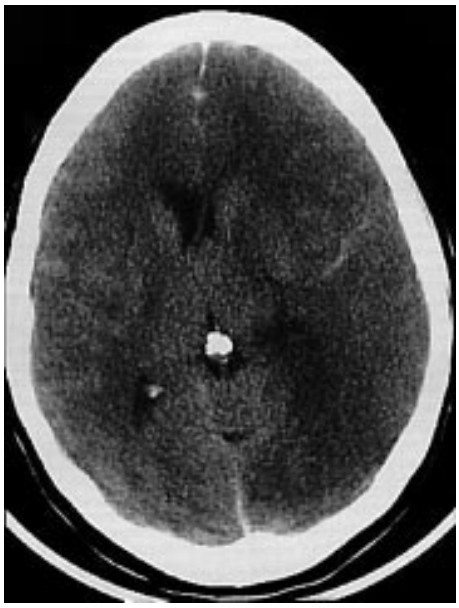

Figure 2 Extensive left hemisphere ischaemia 10 days after the initial subarachnoid haemorrhage from a posterior communicating aneurysm.

CT scans may demonstrate the underlying pathological source of the bleed and any space occupying lesions demanding immediate surgical decompression, including obstructive hydrocephalus. Localisation of blood collections can also assist in targeting the culprit for the haemorrhage where more than one potential source is present (such as multiple intracranial

Table 1 Inflammatory consequences of subarachnoid haemorrhage

- Red cell lysis and release of catalytic agent (e.g. oxyhaemoglobin)
- Free radical generation and lipid peroxidation
- Prostaglandin activation
- Complement activation
- Platelet activation and adhesion
- Release of vasoconstrictive agents:
  - –calcium ions
  - –growth factors
  - –IgG and complement
  - –5 HT, histamine, bilirubin, neuropeptides
- Reduced synthesis of endothelium dependent relaxation factor (EDRF)
- Structural changes to arterial wall media with late fibrosis

5 HT, 5 hydroxytryptamine; EDRF, endothelium derived relaxing factor.

Table 2 Causes of spontaneous subarachnoid haemorrhage

Intracranial aneurysms: degenerative	60–70%
Peri-mesencephalic haemorrhages	15–20%
Arteriovenous malformations and associated aneurysms	5–10%
Other causes:	~ 5%
Dural fistula	
Venous vascular abnormalities	
Spinal arteriovenous malformations	
Cerebral artery dissections	
Moyamoya syndrome	
Vasculopathies	
Mycotic aneurysms	
Coagulopathies	
Neoplasia	
Pituitary apoplexy	
Drug abuse: amphetamine and cocaine	

Table 3 Genetic conditions predisposing to aneurysm formation and subarachnoid haemorrhage

- Adult polycystic kidney disease
- Coarctation of the aorta
- Marfan's syndrome
- Hereditary haemorrhagic telangectasia
- Ehlers–Danlos syndrome
- α1 Antitrypsin deficiency

Table 4 World Federation of Neurosurgeons (WFNS) grading system of subarachnoid haemorrhage

WFNS grade	Glasgow coma score	Focal signs
I	15	–ve
II	13–14	–ve
III	13–14	+ve
IV	7–12	+/-ve
V	3–6	+/-ve

Table 5 The Fisher CT scan grading scale for severity of subarachnoid haemorrhage in relation to ischaemic complications

Group	Subarachnoid blood	Risk of cerebral ischaemia
1	None	Low
2	Diffuse	Only moderate
3	Clot or thick layer	High
4	Blood in lateral ventricles	Low

Table 6 Pathophysiological events following subarachnoid haemorrhage

Systemic
- Pyrexia
- Hypovolaemia
- Hypotension
- Neurogenic pulmonary oedema
- Cerebral salt wasting (natriuretic factor) and hyponatraemia
- Cardiac dysfunction and ECG changes

Cerebral
- Raised intracranial pressure
- Acute hydrocephalus
- Loss of cerebral vessel autoregulation
- Cerebral "vasospasm" and low cerebral blood flow
- Cerebral hypoxia
- Epilepsy

aneurysms). Extracranial signs of injury point towards a traumatic mechanism for SAH, and include soft tissue swelling and skull fractures.

On occasions the CT images are either normal or equivocal. In the face of a convincing history, a lumbar puncture taken 6–12 hours after the ictus (allowing time for red blood cell lysis) should be undertaken for xanthochromic analysis using spectrophotometry.[10] The "three test tube" method with visual interpretation is notoriously unreliable. For those patients who present late (up to three weeks after the ictus) investigations are less urgent but should follow the same sequence. Magnetic resonance imaging (MRI) is of little value for investigation of acute SAH.

For sourcing the SAH, digital subtraction angiography (DSA) remains the gold standard (fig 3). Newer techniques include CT angiography (CTA) (fig 4), MR angiography (MRA) (fig 5), and transcranial colour coded duplex ultrasonography (TCCD) (fig 6). These techniques remove the risks of invasive angiography, but have yet to replace DSA in most units.

MRI and MRA can be helpful in cases of late (over three weeks) presentation where CT scans are normal and there is clinical doubt, and avoids the small risks from invasive DSA. Late MRI/MRA follow up of SAH patients with negative DSA findings is selected for suspected intraparenchymal abnormalities (for example, a small arteriovenous malformation, or venous cavenoma).

MANAGEMENT

General medical care includes surveillance of fluid and salt balance, glucose, and urea, and assessment of cardiovascular and respiratory adequacy. An ECG may demonstrate subendocardial ischaemia. For awake patients pain relief (codeine phosphate 30–60 mg every 4–6 hours) is appropriate; sedation should be avoided. Anti-emetics should be liberally prescribed for retching. Nursing should be in a quiet environment.

For those presenting in coma, the ABC of medical resuscitation is evoked to prevent secondary mechanisms of cerebral injury (hypoxia and hypotension). Paralysis, intubation, and ventilation are mandatory in those unable to protect the airway or self ventilate, and for those in poor grade who need transfer to another hospital. The level of coma and pupillary abnormalities in poor grade patients should largely be ignored in the early phases of resuscitation, as they are often unreliable for prognostic purposes. Accurate grading should therefore be deferred until resuscitation is complete and a CT scan has been obtained, and should only be undertaken within an appropriate environment with all relevant information to hand (usually after a few hours of presenting in an intensive care unit).

Specific medical care demands an understanding of the pathophysiological consequences of SAH.[4] A number of specific events follow SAH (table 6), all of which generate a potential state of delayed cerebral ischaemia (cerebral vasospasm, fig 7) leading to poor cerebral perfusion (fig 8). Fluid resuscitation is designed to address aspects of hypovolaemia, hyponatraemia, and hypotension. Alternating normal saline with colloid is commonly used, providing an input of around 3 litres per 24 hours. In the elderly and comatose patient, more sophisticated means of fluid balance monitoring is required using central venous and pulmonary artery wedge pressure catheters. Cerebral blood flow augmentation using hypervolaemia, haemodilution, and hypertension (with inotropic agents) is reserved for intensive care treatment where invasive monitoring of systemic variables is mandatory.

Nimodipine, a putative neuroprotective agent and cerebral calcium antagonist, is the only agent which has shown clinical benefit by reducing the frequency of delayed cerebral ischaemia.[11] The drug has mild hypotensive properties and should be started (orally 60 mg four times daily) once hypotension has been corrected. For the comatose patient, intravenous nimodipine (1–2 mg/hour) can be considered and titrated against an adequate blood pressure (mean arterial blood pressure ~100 mm Hg). Antifibrinolytic treatment is contraindicated.[12]

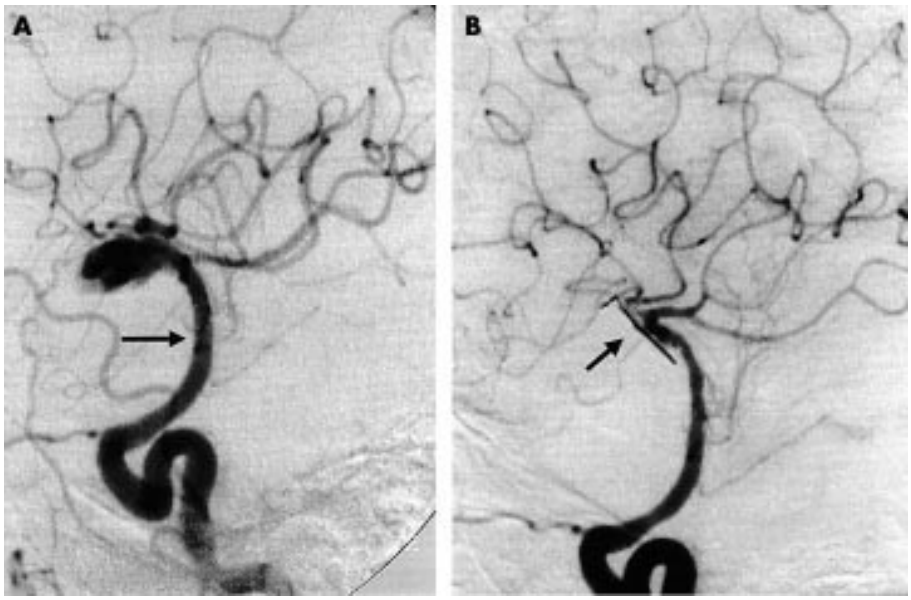

Figure 3 (A) Right carotid digital subtraction angiography (lateral projection) showing middle cerebral artery aneurysm and pronounced mass effect from an intracerebral haematoma. (B) As for (A) following surgical clipping (arrow).

The role of surgery in the acute resuscitation process revolves around the management of raised intracranial pressure (ICP). Insertion of an external ventricular drain is used for reducing hydrocephalus and/or haemocephalus. Urgent salvage procedures to evacuate parenchymal haematomas (before DSA investigation) is reserved for states of acute intracranial decompensation and pupillary abnormalities (fig 1B).

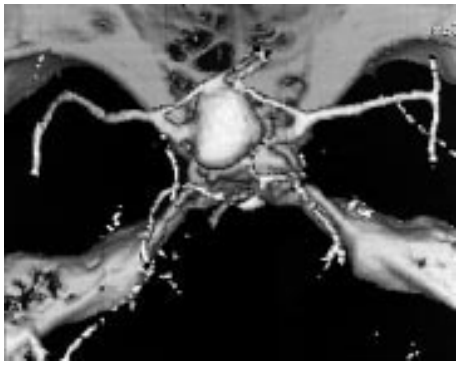

Figure 4 Three dimensional computed tomographic angiography of an anterior communicating aneurysm.

DEFINITIVE TREATMENT

The international cooperative study on SAH indicated that aneurysmal rebleeding was responsible for approximately 30% of deaths and disability.[13] The severity of the initial bleed and delayed cerebral ischaemia accounted for the remaining poor outcomes. Delays in definitive treatment are associated with avoidable deaths.[14] Early definitive treatment of the culprit aneurysm could feasibly salvage up to a third of poor outcomes; with modern methods to secure ruptured intracranial aneurysms, early surgery does not appear to be associated with increased occurrence of cerebral ischaemia. Recent series do not demonstrate worse surgical outcomes with early surgery, supporting a policy towards earlier surgery.[15]

Security of the aneurysm is achieved by direct open surgery and application of a surgical clip (fig 3B), or by endovascular techniques adopting a variety of evolving methods (fig 9).[16]

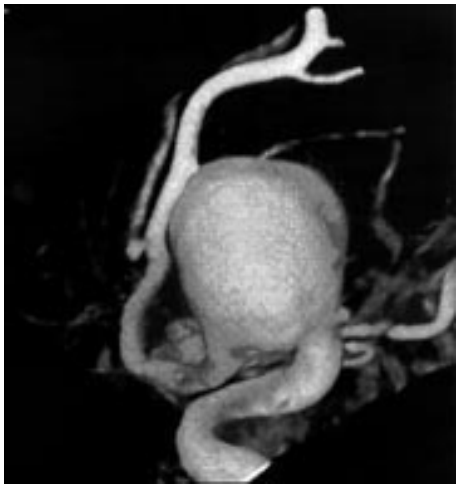

Figure 5 Magnetic resonance angiography of a giant ophthalmic aneurysm.

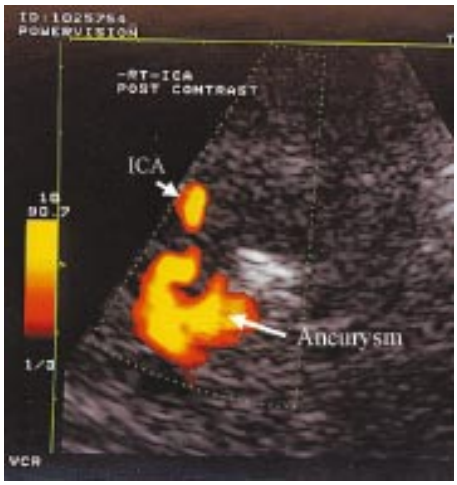

Figure 6 Transcranial colour coded duplex ultrasonography ultrasound image of a posterior communicating aneurysm.

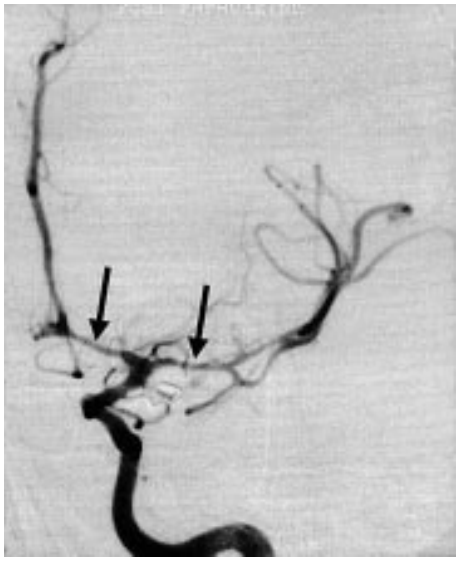

Figure 7 Anterioposterior digital subtraction angiography projection following a left carotid injection. Extensive cerebral vasospasm evident in this poor grade patient.

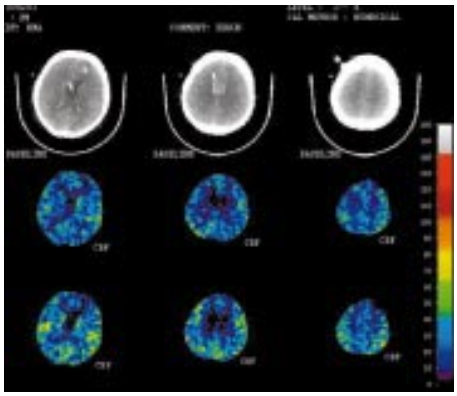

Figure 8 Xenon CT quantified cerebral blood flow scan in a poor grade (WFNS grade 5) patient showing critically low levels of cerebral blood flow.

OUTCOME

With modern treatment for aneurysmal SAH, outcome is largely determined by two key variables—age, and grade of presentation. Although those aged 65 years and over do less well, the majority (75%) undergoing surgery can still expect a favourable outcome.[15 17] Age is no longer a contraindication for definitive treatment. Poor grade patients (WFNS IV and V) generally fair badly with high mortality (85%).[18] However, patients improving from a poor grade to a better grade following resuscitation and drainage of hydrocephalus can expect a favourable outcome in 60% of cases. The poor grade elderly patient invariably dies.[18 19]

UNRUPTURED ANEURYSMS

The prevalence of unruptured intracranial aneurysms has been reported to be 1%.[1 5] The majority are incidental lesions, whereas a small proportion present with consequences of mass effect, epilepsy, or non-specific symptoms such as headaches. The recent international study of unruptured intracranial aneurysms[20] has indicated a spontaneous rupture rate far lower than previously thought, averaging 0.05% per annum. This varies according to aneurysm size, position, and prior history of SAH from a separate lesion. Aneurysms below 10 mm rarely demand attention, whereas larger lesions (especially infratentorial with a prior history of SAH) are more likely to benefit from treatment. Calculations of individual treatment risk/benefit ratio require careful consideration, and should be delegated to the appropriate neurovascular specialist.[21] Giant symptomatic aneurysms (> 25 mm size) are dangerous lesions which should always be considered for treatment, adopting a multidisciplinary approach (figs 4, 5, and 6).

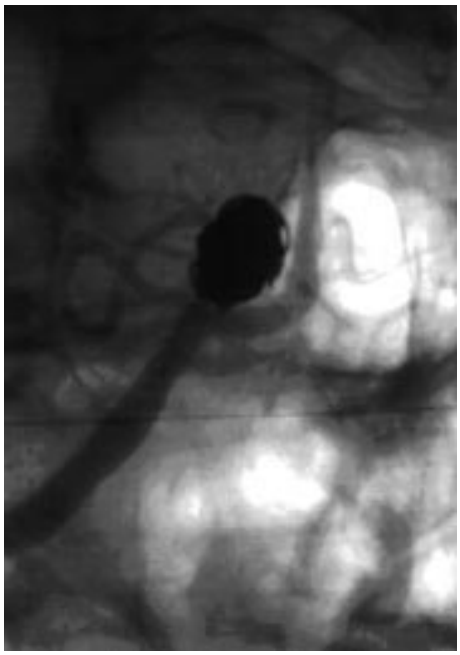

Figure 9 Endovascular coil within a basilar tip aneurysm.

SCREENING FOR INTRACRANIAL ANEURYSMS

Most patients suffering aneurysmal SAH have no relevant family history for the condition, and do not suffer from further events. Screening for future aneurysms is not indicated.[22] Those with a strong family history for SAH, and those with certain genetic disorders (table 2), may be more likely to benefit from screening, but this remains unproven. Although cheap, rapid, and non-invasive outpatient based screening methods may prove helpful (figs 4, 5, and 6), general medical advice concerning vascular risk factors is currently more profitable, with close attention to smoking and hypertension.

REFERENCES

1 **Schievink WI**. Intracranial aneurysms. *N Engl J Med* 1997;**336**:28–40.
2 **Roos YB**, Beenen LF, Groen RJ, *et al*. Timing of surgery in patients with aneurysmal subarachnoid haemorrhage: rebleeding is still the major cause of poor outcome in neurosurgical units that aim at early surgery. *J Neurol Neurosurg Psychiatry* 1997;**63**:490–3.
3 **Broderick JP**, Brott TG, Duldner JE, *et al*. Initial and recurrent bleeding are the major causes of death following subarachnoid hemorrhage. *Stroke* 1994;**25**:1342–7.
4 **Findlay JM**, Macdonald RL, Weir BKA. Current concepts of pathophysiology and management of cerebral vasospasm following subarachnoid hemorrhage. *Cerebrovasc Brain Metab Rev* 1991;**3**:336–61.
5 **Stehbens WE**. Etiology of intracranial berry aneurysms. *J Neurosurg* 1989;**70**:823–31.
6 **Longstreth WT**, Koepsell TD, Yerby MS, *et al*. Risk factors for subarachnoid haemorrhage. *Stroke* 1985;**16**:377–85.

7 **Teasdale GM**. A universal subarachnoid haemorrhage scale: report of a committee of the World Federation of Neurological Societies. *J Neurol Neurosurg Psychiatry* 1988;**51**:1457.
8 **van der Wee N**, Rinkel GJ, Hasan D, *et al*. Detection of subarachnoid haemorrhage on early CT: is lumbar puncture still needed after a negative scan? *J Neurol Neurosurg Psychiatry* 1995;**58**:357–9.
9 **Fisher CM**, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. *Neurosurgery* 1980;**6**:1–9.
10 **Vermeulen M**, van Gijn J. The diagnosis of subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry* 1990;**53**:365–72.
11 **Pickard JD**, Murray GD, Illingworth R, *et al*. Effect of oral nimodipine on cerebral infarction and outcome after subarachnoid haemorrhage: British aneurysm nimodipine trial. *BMJ* 1989;**298**:636–42.
12 **Vermeulen M**, Lindsay KW, Cheah MF, *et al*. Antifibrinolytic treatment in subarachnoid haemorrhage. *N Engl J Med* 1984;**311**:432–7.
13 **Kassell NF**, Torner JC, Haley EC, *et al*. The international cooperative study on the timing of aneurysm surgery. Part 1: overall management results. *J Neurosurg* 1990;**73**:18–36.
14 **Hutchinson PJA**, Seeley HM, Kirkpatrick PJ. Factors implicated in deaths from subarachnoid haemorrhage: are they avoidable? *Br J Neurosurg* 1998;**12**:37–40.
15 **Ross N**, Hutchinson PJA, Seely H, *et al*. Timing of surgery for supratentorial aneurysmal subarachnoid haemorrhage – report of a prospective study. *J Neurol Neurosurg Psychiatry* 2002;**72**:480–4.
16 **Byrne JV**. Endovascular treatments for intracranial aneurysms [review]. *Br J Radiol* 1996;**69**:891–9.
17 **Hutchinson PJA**, Kirkpatrick PJ. The diagnosis of subarachnoid haemorrhage in the elderly. *Geriatric Med* 1997;**27**:1–3.
18 **Hutchinson PJA**, Power DM, Tripathi P, *et al*. Outcome from poor grade aneurysm subarachnoid haemorrhage – which poor grade subarachnoid haemorrhage patients benefit from aneurysm clipping? *Br J Neurosurg* 2000;**14**:105–9.
19 **Bailes JE**, Spetzler RF, Hadley MN, *et al*. Management morbidity of poor-grade aneurysm patients. *J Neurosurg* 1990;**72**:559–66.
20 **International Study of Unruptured Intracranial Aneurysms Investigators**. Unruptured intracranial aneurysms: risk of rupture and risks of surgical intervention. *N Engl J Med* 1998;**339**:1725–33.
21 **Kirkpatrick PJ**. Time to reconsider treatment options of intracranial aneurysms. *Lancet* 1999;**353**:942–3.
22 **Kirkpatrick PJ**, McConnell RS. Screening for familial intracranial aneurysms *BMJ* 1999;**319**:1512–3.