Intracranial haemorrhage

Increasing use of antiplatelet medication has led to an increase in intracranial haemorrhage as a cause of stroke over the past decade.

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Intracranial haemorrhage accounts for 15 - 20% of strokes[1] and has risen in incidence by 18% over the past 10 years to 24.6/100 000.[2] This has been ascribed to increased use of antiplatelet and anticoagulant medication for conditions such as atrial fibrillation, as well as an ageing population with untreated hypertension and diabetes.[3] Because this increase in incidence has also occurred in low-to-middle income countries, one can anticipate an increased incidence in South Africa. Subarachnoid haemorrhage is a less common form of stroke than hypertensive haemorrhage, with an incidence of 6 - 7/100 000.[4]

Intracranial haemorrhage is caused by extravasation of blood from an artery, capillary or vein. If the vessel lies in the subarachnoid space, the haemorrhage is referred to as a subarachnoid haemorrhage (SAH). If the vessel is in the parenchyma of the brain the haemorrhage is referred to as an intracerebral or intraparenchymal haemorrhage or haematoma (ICH). There may be crossover with an SAH having an ICH and *vice versa*. Either may result in blood in the ventricles – an intraventricular haemorrhage (IVH). The causes of intracranial haemorrhage are listed in Table 1.

Certain conditions such as polycystic kidney disease and Ehlers Danlos syndrome predispose to aneurysms.

Pathophysiology

ICH is usually from small-vessel disease, i.e. penetrating vessels in the 50 - 700 µm region (Fig. 1). Hypertension results in breakage of the elastic lamina, atrophy and fragmentation of the smooth muscle with fibrinoid necrosis and the formation of micro-aneurysms, also known as Charcot Bouchard aneurysms.

In amyloid angiopathy there is deposition of amyloid-β in the capillary wall, which also results in microaneurysm formation, concentric splitting, chronic inflammatory infiltrates and fibrinoid necrosis.

Only one stroke in every 20 is an SAH,[1] while 85% of SAH are secondary to an aneurysm, with 10% from so-called peri-mesencephalic bleeds and the remaining 5% from other rare causes. In the vast majority of cases, SAH is due to a ruptured aneurysm in the subarachnoid space. 'Berry' aneurysms occur where there is a defect in the media of the arterial wall and are typically seen in the anterior circulation. However, in the posterior circulation aneurysms tend to show dissection, where there is haemorrhage into the medial layer of the vessel wall. Certain conditions such as polycystic kidney disease and Ehlers-Danlos syndrome predispose to aneurysms.

Risk factors

The most important risk factor for an intracranial bleed is hypertension – this is an even stronger risk factor than for ischaemic stroke. Treatment of hypertension reduces the risk from 2.9/100 000 to 1.9/100 000.

Table 1. Causes of intracranial haemorrhage

Intracerebral haematoma	Subarachnoid haemorrhage
Hypertensive haemorrhage	Aneurysm
Amyloid angiopathy	Peri-mesencephalic bleed
Arterio-venous malformation	Arterio-venous malformation
Aneurysmal haemorrhage	Pituitary apoplexy
Haemorrhagic tumour	Drug abuse
Dural sinus fistula	Anticoagulant drugs
Infarct with haemorrhagic transformation	Pituitary apoplexy
Venous infarct with haemorrhagic transformation	Anticoagulant drugs

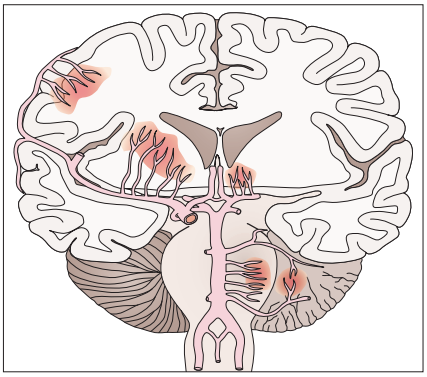

Fig. 1. Common sites of hypertensive haemorrhage from penetrating vessels.

Other risk factors include:[1,2]

- smoking – less so than for ischaemic stroke, but related to number of cigarettes smoked per day
- obesity – increased waist-to-hip ratio rather than body mass index
- diet – increased with red meat/organ meat/eggs/pizza/fried food, but reduced by fruit and nuts
- regular activity reduces all forms of stroke
- alcohol consumption has no association if less than 30 drinks per month
- psychological stress is a risk factor.

Modifiable risk factors for subarachnoid haemorrhage are hypertension, smoking and excessive alcohol intake, all of which almost double the risk.[5] Screening of patients for aneurysms should only be carried out if there is a history of two first-degree relatives having had SAH from aneurysms.[6]

Clinical presentation

Presentation depends on the type of intracranial bleed and the site and size of the haemorrhage. Hypertensive bleeds in the basal ganglia may present with a hemiplegia, while brainstem bleeds tend to be more devastating, with typically a low Glasgow coma score (GCS) from the onset. Cerebellar haemorrhage may present with cerebellar signs and symptoms or with raised intracranial pressure due to hydrocephalus.

Patients with amyloid angiopathy may have dementia preceding the haemorrhage. Arteriovenous malformation (AVM) bleeds are seen more often in younger patients, who often have a better GCS than the extent of the haemorrhage would suggest.

Patients who have an aneurysmal SAH present with the classic thunderclap headache. Between 25% and 30% of SAH patients die with the initial haemorrhage. Those who survive are at greatest risk of a re-bleed in the first 48 hours and have a re-haemorrhage rate of 24% in the first 14 days if the aneurysm is not treated.

Diagnosis

Usually the diagnosis is made on a non-contrasted computer tomography (CT) scan as blood, being hyperdense on CT, is easy to identify (Fig. 2). Furthermore, a CT angiogram (CTA) can be done, which will help diagnose conditions such as a cerebral aneurysm, an AVM and a venous infarct with haemorrhagic transformation. Up to 15% of patients will show a cause on CTA[7] (Fig. 3).

MRI is as good as CT scan in diagnosing ICH.[8] The imaging characteristics of blood vary with age. In the acute phase gradient-recalled-echo imaging with T2-weighted images are best.[9] MRI may also be used, either in the acute phase or later to reveal other underlying causes that may not be easily diagnosed on CT or CTA, such as cavernomas or haemorrhagic transformation of underlying tumour (Figs 4 and 5).

In a patient who has a negative CT scan but has a history typical for an aneurysmal SAH, a lumbar puncture will rarely disclose xanthochromic CSF, which is diagnostic for SAH. Alternatively, in a suggestive history a CTA may be done and any patient who has an SAH with a negative CTA should have a digital subtraction angiogram (DSA) before discharge.

Diagnosis, as discussed earlier, relies on a history in keeping with an ictus, appropriate findings of subarachnoid blood in imaging and then CTA or MRA. CTA is 95% accurate at detecting aneurysms.[10] If the index of suspicion is high and the CT is negative

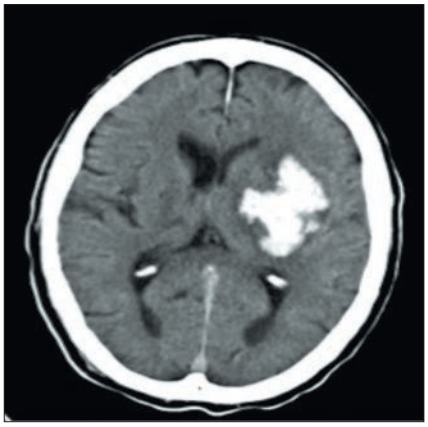

Fig. 2. A hypertensive patient who presented with sudden-onset left-sided weakness and dysphasia. The bleed is in the left basal ganglia most often originating in the putamen.

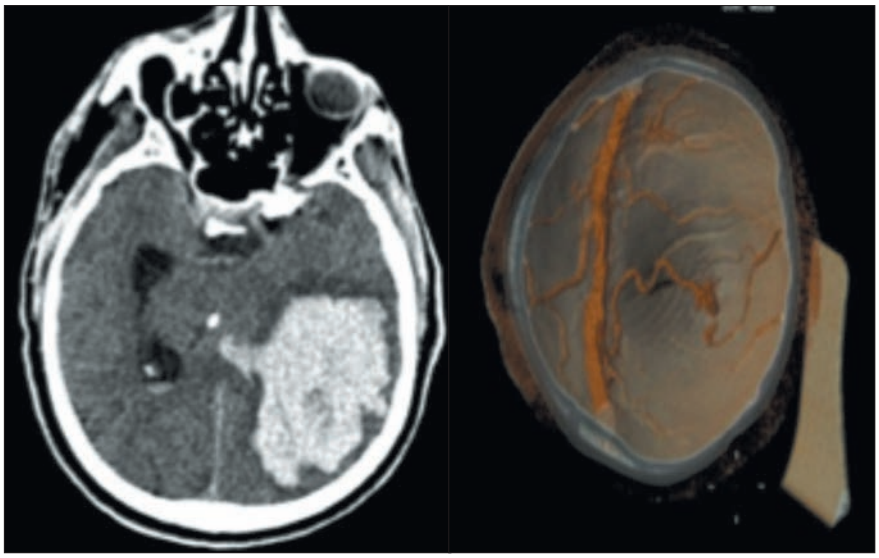

Fig. 3. This 26-year-old patient presented with sudden-onset headache, right-sided weakness and dysphasia. Even though there was mass effect from the haematoma the CTA still showed a large draining vein from the AVM.

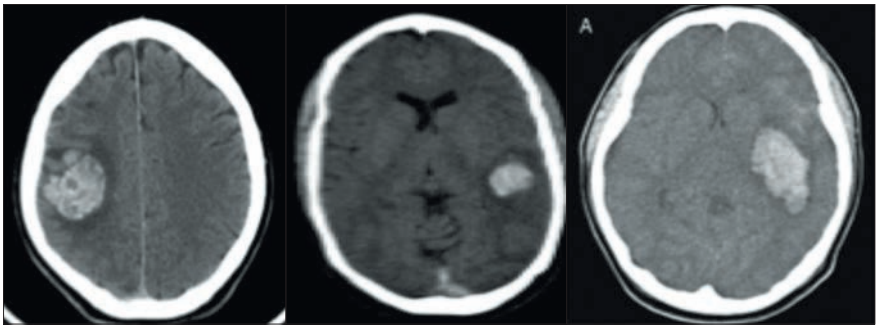

Fig. 4. CT scans of three different patients with three similar-looking parietal intracranial haematomas.

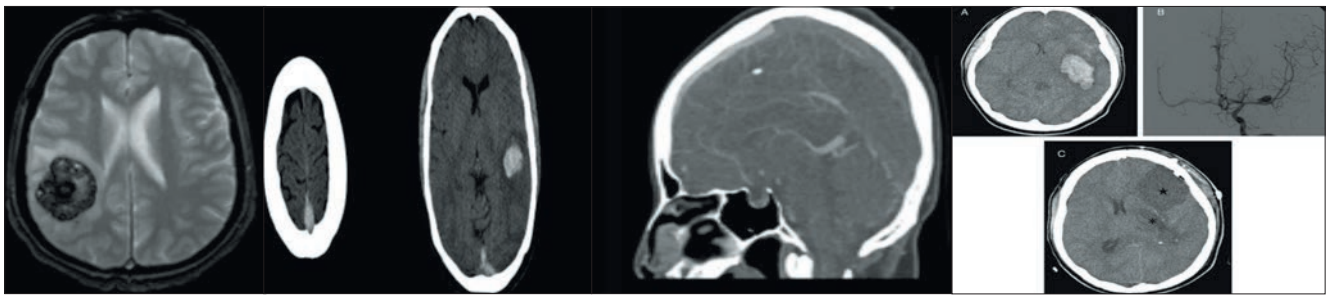

Fig. 5. Further imaging of the patients in Fig. 4. A gradient echo MRI reveals a cavernoma on the image on the left, the middle image is a CTV showing thrombosis of the superior saggital sinus and the image on the right is the DSA, which showed the MCA aneurysm.

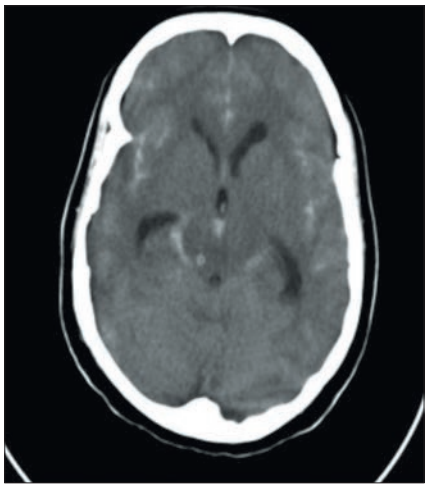

Fig. 6. Uncontrasted CT scan of a patient showing an SAH with blood in the interhemispheric, Sylvian and ambient cisterns. The temporal horns of the ventricular system are enlarged.

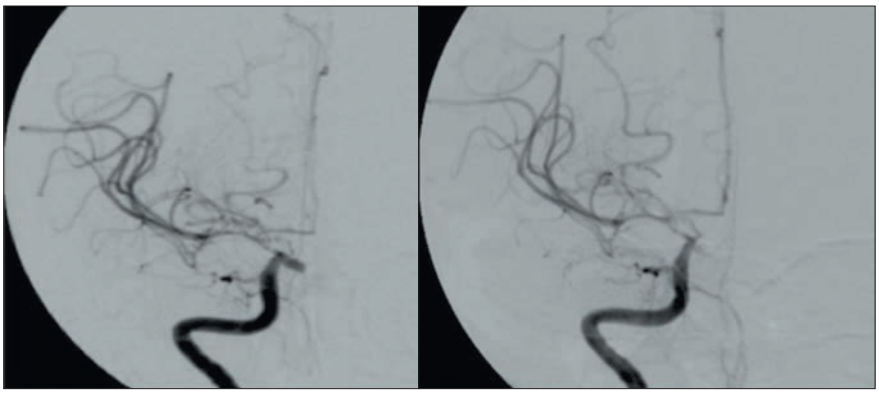

Fig. 7. DSA of the patient in Fig. 6 showing a medially pointing ICA aneurysm both pre- and post-coiling. Note the vasospasm of the IC distal to the aneurysm in both the anterior and middle cerebral arteries.

a lumbar puncture should be done if the patient is suitable. A negative CTA in the face of xanthochromia or a negative CTA in the face of SAH on CT warrants a DSA. The importance of pursuing the diagnosis and actively excluding an aneurysm is that in a missed aneurysm that could have been treated, a re-bleed carries a morbidity and mortality close to 80% (Figs 6 and 7).[11]

Further investigations include full blood count, electrolytes, glucose, liver function tests and a clotting profile, especially if the patient has a history of being on anticoagulants.

Acute management

Management of an intracranial haemorrhage can be divided into the acute management and subsequent definitive management, which depends on the cause of the haemorrhage.

The initial treatment goals for an intracranial haemorrhage are to stabilise the patient and prevent further neurological deterioration:

- intubation if GCS ≤8
- raise head 30 - 40 degrees, position the neck straight and loosen anything constricting around the neck to optimise venous outflow
- blood pressure (BP) control should be individualised to each patient according to their BP history and their type of bleed.

Controlling BP in these patients is to prevent both further haemorrhage if the BP is too high as well as secondary neurological damage if it is too low. If the patient has raised intracranial pressure aim for a mean arterial blood pressure (MAP) above 60 mmHg. Haematoma growth is a strong predictor of 30-day mortality.[12] Of the patients who have an ICH, 38% experience haematoma 'growth' of at least 33%. ICH growth is associated with neurological deterioration.[13] Because of the worse outcomes associated with a large ICH, BP reduction to limit growth seems intuitive, but studies have not been conclusive. The ATACH and INTERACT trials seemed to suggest that ICH enlargement was reduced when the MAP was treated to 150 mm Hg.[14,15] These trials are ongoing and the current recommendations are to treat an SBP >200 mmHg or a mean arterial pressure >150 mmHg.

Another tempting method of preventing ICH growth is the use of haemostatic therapy. Recombinant factor VIIa (rFVIII),

a haemostatic drug used for haemophilia, has been studied as a possible drug to limit ICH growth. Although ICH was reduced in patients who received the drug, there was no significant difference seen in the proportion of patients with poor clinical outcome.[16] Therefore, rFVIIa seems to reduce haematoma growth but does not improve survival or functional outcome.

A patient who is on anticoagulant therapy should have this rapidly corrected, as some investigators believe this prevents continued bleeding.[17]

Definitive management

Intracerebral haematoma

Surgical management can be divided into surgical procedures that indirectly address the ICH, such as placement of an intracranial pressure monitor or an external ventricular drain for hydrocephalus, and those that directly address the ICH.

Surgical procedures addressing the ICH directly have not turned out to be as favourable as one might expect. The Surgical Trial in Intracerebral Hemorrhage (STICH) was an international, prospective, randomised trial comparing early surgery and initial conservative management in 1 033 patients with spontaneous supratentorial ICH for whom best treatment was deemed uncertain.[18] The study end-point was favourable clinical outcome, which was defined as good recovery or moderate disability on the Glasgow Outcome Scale. No significant difference was seen between groups, with favourable outcome achieved in 26% of patients randomised to early surgery compared with 24% of patients randomised to conservative treatment. The authors concluded that early surgical evacuation of IPH showed no overall benefit compared with conservative medical therapy. However, a subset of patients with haematomas less than 1 cm from the cortical surface may benefit from surgical evacuation. This, together with criticism of various limitations of the STICH trial, has led to the initiation of STICH II.[19]

Intracranial haematomas may also be dealt with during another definitive procedure, such as removal of an AVM, haemorrhagic tumour, cavernoma or clipping of an aneurysm.

Prognosis

The ICH score was devised by Hemphill and colleagues and helps predict 30-day mortality by looking at features such as age, ICH volume, the presence or absence of IVH, GCS and ICH position.[20] The 30-day mortality ranges from 35% to 52%, with only 20% of survivors expected to make a full functional recovery in 6 months.[21]

Subarachnoid haemorrhage

SAH has a high morbidity and mortality. The case fatality after aneurysmal haemorrhage is 50% – 1 in 8 patients with subarachnoid haemorrhage dies outside hospital.[5] It is important to make the diagnosis urgently because of the high re-haemorrhage rate associated with SAH. In the first few hours after the initial haemorrhage, up to 15% of patients have a sudden deterioration of consciousness that suggests re-bleeding. This culminates in a re-bleeding rate approaching 40% in untreated aneurysms at 4 weeks.[22]

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Endovascular coiling of aneurysms has largely replaced surgical clipping. The International Subarachnoid Aneurysm Trial (ISAT) looked at 2 143 patients randomised to coiling or clipping and was stopped early when it became clear that the relative risk reduction for poor outcome (death or dependency) for coiling versus clipping was 24% (95% CI 12 - 33%).[23] The absolute risk reduction of poor outcome was 7% (4 - 11%). Subsequent studies have supported these findings. Subsequent to ISAT the devices utilised in coiling aneurysms have improved. ISAT II will look at these devices, again comparing their use to clipping. Clipping of aneurysms is still a good way of treating aneurysms and if this is the only modality it is better to use this, rather than wait. Complex aneurysms such as those with wide necks or branches originating from the neck (as often seen with MCA aneurysms) may be better managed with surgical clipping.

Subsequent to securing the aneurysm, the biggest cause of morbidity and mortality is from vasospasm and delayed cerebral ischaemia. This is treated with fluids, oxygen and calcium channel blockers and, on occasion, by endovascular angioplasty. The only other surgical intervention may be the placement of an external ventricular drain or ventriculo-peritoneal shunt for hydrocephalus.

Prognosis

SAH is a devastating disease with a high morbidity and mortality. In those patients who are perceived to have a good outcome and who are perceived to be normal, only 25% of those independent in activities of daily living report a complete recovery without psychosocial or neurological problems.[24]

Conclusion

Intracranial haemorrhage will continue to increase in frequency. The haemorrhage is the clinical and radiological manifestation of an underlying disease process, which needs to be identified so the correct treatment is given. While two haematomas may look the same, their causes may be different and their subsequent management may be completely different.

So, when confronted with a patient with an intracranial haemorrhage, how do you

decide which patients warrant further investigation? As a patient's age increases, the yield of angiographic causes of an ICH decreases, with a cut-off at the age of 45 years. In hypertensive patients the yield is low. Patients with IVH, particularly without ICH, patients with lobar haemorrhages and patients with SAH need investigation. In essence, a hypertensive patient older than 45 years with an ICH in the basal ganglia, thalamus or posterior fossa does not require further investigation, but any other ICH does.

References

1. Caceres JA, Goldstein JN. Intracranial haemorrhage. Emerg Med Clin N Am 2012;30:771-794. [http://dx.doi.org/10.1016/j.emc.2012.06.003]
2. Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. Lancet 2009;373(9675):1632-1644. [http://dx.doi.org/10.1016/S0140-6736(09)60371-8]
3. Feigin VL, Lawes CMM, Bennett DA, Anderson CS. Stroke epidemiology: A review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. Lancet Neurol 2003;2:43-53. [http://dx.doi.org/10.1016/S1474-4422(03)00266-7]
4. Van Gijn J, Kerr RS, Rinkel GJ. Subarachnoid haemorrhage. Lancet 2007;369:306-318. [http://dx.doi.org/10.1016/S0140-6736(07)60153-6]
5. Feigin VL, Rinkel GJE, Lawes CM, et al. Risk factors for subarachnoid hemorrhage: An updated systematic review of epidemiological studies. Stroke 2005;36:2773-2780. [http://dx.doi.org/10.1093/brain/awh497]
6. Teasdale GM, Wardlaw JM, White PM, Murray G, Teasdale EM, Easton V. The familial risk of subarachnoid haemorrhage. Brain 2005;128:1677-1685. [http://dx.doi.org/10.3174/ajnr.A1546]
7. Delgado Almandoz JE, Schaefer PW, Forero NP, et al. Diagnostic accuracy and yield of multidetector CT angiography in the evaluation of spontaneous intraparenchymal cerebral hemorrhage. Am J Neuroradiol 2009;30(6):1213-1221. [http://dx.doi.org/10.1001/jama.292.15.1823]
8. Kidwell CS, Chalela JA, Saver J, et al. Comparison of MRI and CT for detection of acute intracerebral hemorrhage. JAMA 2004;292(15):1823-1830. [http://dx.doi.org/10.1016/j.rcl.2010.07.011]
9. Smith SD, Eskey CJ. Hemorrhagic stroke. Radiol Clin North Am 2011;49(1):27-45. [http://dx.doi.org/10.1016/j.rcl.2010.07.011]
10. Chappell ET, Moure FC, Good MC. Comparison of computed tomographic angiography with digital subtraction angiography in the diagnosis of cerebral aneurysms: A meta-analysis. Neurosurgery 2003;52:624-630. [http://dx.doi.org/10.1227/01.NEU.0000047895.82857.EB]
11. Roos YBWEM, de Haan RJ, Beenen LFM, Groen RJM, Albrecht KW, Vermeulen M. Complications and outcome in patients with aneurysmal subarachnoid haemorrhage: A prospective hospital based cohort study in The Netherlands. J Neurol Neurosurg Psychiatry 2000;68:337-341. [http://dx.doi.org/10.1136/jnnp.68.3.337]
12. Aguilar MI, Freeman WD. Treatment of coagulopathy in intracranial hemorrhage. Curr Treat Options Neurol 2010;12(2):113-128. [http://dx.doi.org/10.1007/s11940-010-0061-1]
13. Brott T, Broderick JP, Kothari R, et al. Early hemorrhage growth in patients with intracerebral hemorrhage. Stroke 1997;28:1-5. [http://dx.doi.org/10.1161/01.STR.28.1.1]
14. Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) Investigators. Antihypertensive treatment of acute cerebral hemorrhage. Crit Care Med 2010;38(2):637-648. [http://dx.doi.org/10.1097/CCM.0b013e3181b9e1a5]
15. Anderson CS, Huang Y, Wang JG, et al. INTERACT Investigators. Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT): A randomised pilot trial. Lancet Neurol 2008;7(5):391-399. [http://dx.doi.org/10.1016/S1474-4422(08)70069-3]
16. Mayer SA, Brun NC, Begtrup K, et al. Efficacy and safety of recombinant activated factor VII for acute intracerebral hemorrhage. N Engl J Med 2008;358(20):2127-2123. [http://dx.doi.org/10.1056/NEJMoa0707534]
17. Aguilar MI, Hart RG, Kase CS, et al. Treatment of warfarin-associated intracerebral hemorrhage: Literature review and expert opinion. Mayo Clin Proc 2007;82(1):82-92. [http://dx.doi.org/10.1016/S0025-6196(11)60970-1]
18. Mendelow AD, Gregson BA, Fernandes HM, et al. STICH investigators. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): A randomised trial. Lancet 2005;365(9457):387-397. [http://dx.doi.org/10.1016/S0140-6736(05)17826-X]
19. Mendelow AD, Gregson B, Mitchell P, et al. Surgical trial in lobar intracerebral haemorrhage (STICH II) protocol. Trials 2011;12(1):124. [http://dx.doi.org/10.1186/1745-6215-12-124]
20. Hemphill JC, Bonovich DC, Besmertis L, et al. The ICH score: A simple, reliable grading scale for intracerebral hemorrhage. Stroke 2001;32:891-897. [http://dx.doi.org/10.1161/01.STR.32.4.891]
21. Broderick J, Connolly S, Feldmann E, et al. Guidelines for the management of spontaneous intracerebral hemorrhage in adults. Stroke 2007;38(6):2001-2023. [http://dx.doi.org/10.1161/STROKEAHA.107.183689]
22. Brilstra EH, Algra A, Rinkel GJE, Tulleken CAF, van Gijn J. Effectiveness of neurosurgical clip application in patients with 92 aneurysmal subarachnoid hemorrhage. J Neurosurg 2002;97:1036-1041. [http://dx.doi.org/10.3171/jns.2002.97.5.1036]
23. Molyneux A, Kerr R, Stratton I, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: A randomised trial. Lancet 2002;360:1267-1274. [http://dx.doi.org/10.1016/S0140-6736(02)11314-6]
24. Wermer MJH, Kool H, Albrecht KW, Rinkel GJE. Aneurysm Screening after Treatment for Ruptured Aneurysms Study Group. Subarachnoid hemorrhage treated with clipping: Long-term effects on employment, relationships, personality, and mood. Neurosurgery 2007;60:91-98.

In a nutshell

- Intracranial haemorrhage is caused by extravasation of blood from an artery, a capillary or a vein.
- If the vessel lies in the subarachnoid space, the haemorrhage is referred to as a subarachnoid haemorrhage (SAH).
- If the vessel is within the parenchyma of the brain the haemorrhage is referred to as an intracerebral or intraparenchymal haemorrhage or haematoma (ICH).
- There may be crossover with an SAH having an ICH and vice versa. Either may result in blood in the ventricles – an intraventricular haemorrhage (IVH).
- The most important risk factor for an intracranial bleed is hypertension – this is an even stronger risk factor than for ischaemic stroke.
- Modifiable risk factors for subarachnoid haemorrhage are hypertension, smoking and excessive alcohol intake, all of which almost double the risk.
- Presentation depends on the type of intracranial bleed and the site and size of the haemorrhage.
- Usually the diagnosis is made on a non-contrasted computer tomography (CT) scan as blood, being hyperdense on CT, is easy to identify.
- Management of an intracranial haemorrhage can be divided into the acute management and subsequent definitive management, which depends on the cause of the haemorrhage.