# Management problems of spontaneous ICH

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***The management of spontaneous intracerebral haemorrhage (ICH) can be challenging for hospital doctors. Although the management of ICH is covered in stroke guidelines, many difficult clinical questions remain. In this article the authors suggest approaches to ten common and difficult questions.***

Spontaneous intracerebral haemorrhage (ICH) accounts for 10–15% of all cases of stroke. Populations with a high frequency of hypertension, such as people of Chinese and Japanese ancestry, have higher frequencies of ICH because hypertension is the most common cause of ICH. Less common causes are cerebral amyloid angiopathy, bleeding diatheses, drugs and trauma (*Table 1*). Prognosis following ICH is worse than cerebral infarction, with more than 60% of people with ICH dead at 12 months, two thirds of these in the first month. Less than half of those surviving ICH regain independence in activities of daily living.

The general management of ICH is similar to that for cerebral infarction, e.g. admission to hospital, management in a stroke unit, and attention to swallowing, continence and immobility issues. However, for hospital clinicians, the available stroke guidelines do not always address difficult issues about management of patients with ICH. Examples include, how to manage ICH patients with conditions where antiplatelet or anticoagulant agents would normally be indicated, such as deep venous thrombosis (DVT), pulmonary embolism (PE), atrial fibrillation (AF) and prosthetic heart valves, or where the patient has ischaemic cerebrovascular or cardiovascular disease. Substantial uncertainty about best practice exists in these areas, reflecting the paucity of good trial evidence.

This article suggests management approaches to ten of the most common and difficult questions asked about ICH. Readers are referred to reviews (Qureshi et al, 2001) and guidelines (Broderick et al 1999; Stroke Foundation of New

**TABLE 1.**
**Common causes of intracerebral haemorrhage (ICH)**

| Cause of ICH | Clinical features |
|---|---|
| Hypertensive (*Figure 1*) | Hypertension accounts for 70% of all spontaneous ICH, suggested by bleeding deep in the brain or posterior fossa |
| Cerebral amyloid angiopathy (*Figure 2*) | Generally occurs in patients aged >70 years, usually results in lobar and/or peripheral bleeding |
| AVM (*Figure 3*), cavernoma | History of previous event in same part of the brain, e.g. seizures, headaches. Often occurs in younger patients with no other risk factors for ICH |
| Tumour | Common cancers that metastasize to the brain and bleed are lung, breast and melanoma |
| Trauma | A history of trauma is not always clear. Symptoms may support diffuse brain involvement rather than focal deficit. Imaging for soft tissue or bony abnormality may help |
| Drugs | Particularly chronic heavy alcohol use, cocaine and amphetamines |
| Haemorrhagic transformation following cerebral infarction | Stroke syndrome followed by sudden deterioration in first few days. Repeat brain imaging is necessary to confirm diagnosis. |
| Coagulopathy | Generally, patients on anticoagulant therapy.12% of all spontaneous ICH occurs in people taking warfarin |

AVM = Arteriovenous malformation

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Zealand, 2003; Royal College of Physicians, 2004) for background information and important treatment recommendations.

## QUESTION 1: WHAT SHOULD THE HAEMORRHAGE BE CALLED IN THE CLINICAL NOTES AND/OR DISCHARGE SUMMARY?

Some authors make a distinction between primary and secondary spontaneous ICH. The term 'primary ICH' is usually used to describe ICH resulting from hypertension or amyloid angiopathy. 'Secondary ICH' is used to describe ICH resulting from other causes, such as vascular malformations, tumours or coagulation problems. It is probably best to use the general term 'spontaneous ICH' and qualify this by describing the likely or known aetiology, e.g. 'spontaneous ICH, likely hypertensive' or 'spontaneous ICH, secondary to right temporal arteriovenous malformation (AVM)'.

The term 'haemorrhagic stroke' causes confusion and should be avoided. It is often used as a synonym for ICH but can also mean haemorrhagic transformation of an acute ischaemic stroke. The authors prefer to use 'haemorrhagic transformation' where the clinical situation and brain imaging support a diagnosis of cerebral infarction followed by subsequent bleeding into the infarct.

## QUESTION 2: WHAT IS THE BEST WAY TO DIAGNOSE ICH?

The only sure way of diagnosing ICH is early brain imaging. While headache and an early depression in the level of consciousness are more common in ICH, there is insufficient predictive value in any group of symptoms to enable a reliable clinical distinction between ICH and cerebral infarction. Brain imaging is recommended in all stroke patients unless this would make no difference to clinical management, e.g. when the patient is dying. In most hospitals this is done with computed tomography (CT) scanning. Magnetic resonance imaging (MRI) also accurately identifies ICH and is more useful than CT in recognizing chronic lesions (Fiebach et al, 2004). MRI may also show subclinical 'microbleeds', which may suggest underlying cerebral amyloid angiopathy.

## QUESTION 3: WHAT OTHER INVESTIGATIONS ARE REQUIRED?

A good history and general clinical examination are important in considering possible causes of intracerebral bleeding, including trauma, tumour, vasculitis and drugs (especially cocaine, amphetamines and alcohol). A coagulation screen is appropriate in most patients, including, at least, platelet count, bleeding time, international normalized ratio (INR), and activated partial thromboplastin time. The comprehensiveness of a coagulation screen will be influenced by patient age and any personal or family history of bleeding problems.

To some extent, the cause of an ICH can be inferred from the age and risk profile of a patient and the location of the ICH. For example, cerebral amyloid angiopathy tends to cause lobar haemorrhages in patients older than 70 years, often with underlying cognitive impairment. In contrast, up to one third of patients younger

*Figure 1. Deep cerebral haemorrhage in a man with history of treated hypertension.*

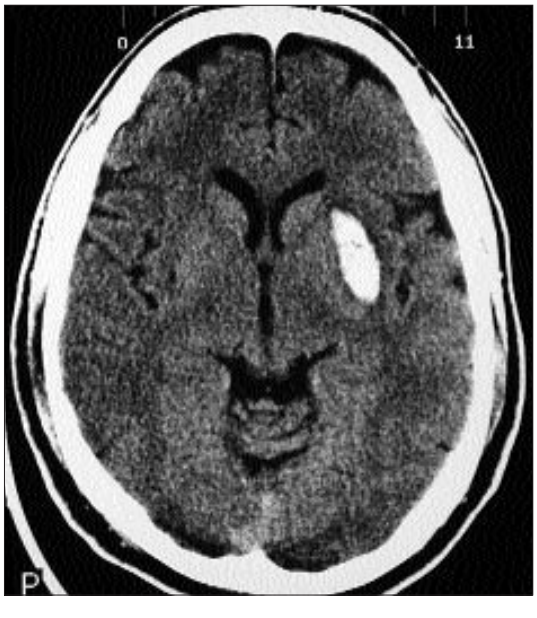
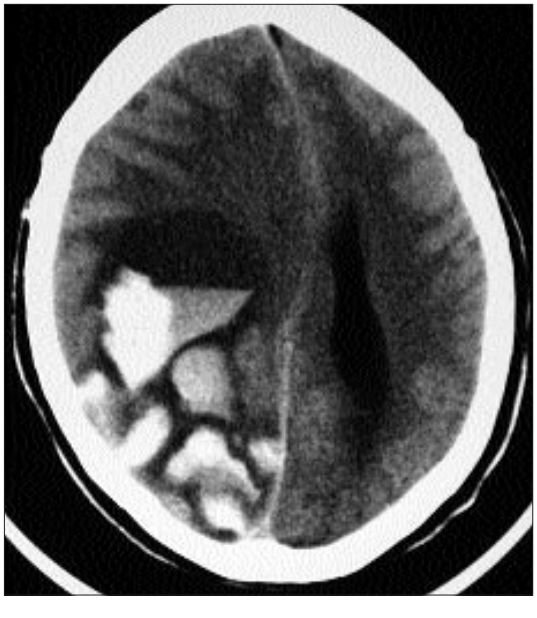



*Figure 2. Lobar haemorrhage in an elderly woman, who collapsed while out shopping.*



than 45 years will have 'secondary' causes for the ICH, such as AVMs and tumours, and more extensive and potentially-invasive investigations need to be considered in this group, particularly if the patient has none of the usual ICH risk factors.

MR angiography (MRA) is reducing the need for invasive cerebral angiography in ICH. Cerebral angiography is generally unnecessary. The yield of angiography in elderly patients with lobar haemorrhage or patients older than 45 years with a history of hypertension is very low and therefore it may be deferred unless a CT or MRI scan suggests an underlying lesion. Where there is doubt about an underlying lesion, an alternative, less invasive approach may be to repeat the CT or MRI after 6–12 weeks.

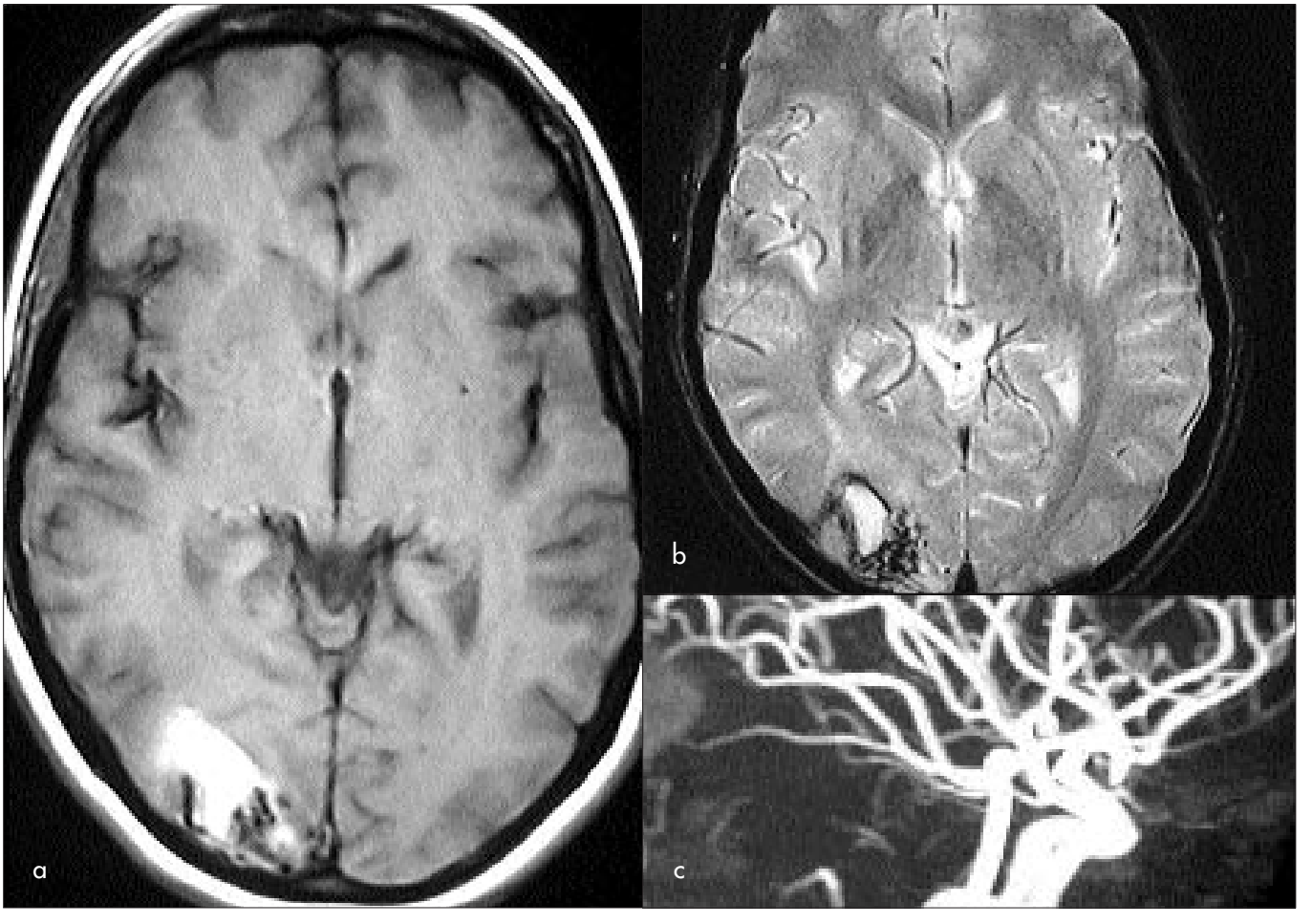
## QUESTION 4: WHO SHOULD BE REFERRED URGENTLY FOR A NEUROSURGICAL EVALUATION?

The group of patients that seem to benefit most from surgery are those with cerebellar haematomas with reduced level of consciousness (Glasgow coma score <14) and/or haematoma diameter >3 cm (Qureshi et al, 2001). Surgical evacuation or decompressive craniectomy in patients with supratentorial haematomas has not been shown to be of benefit. Surgical intervention in this situation is sometimes considered as a 'heroic' last throw of the dice but, if the patient survives, the residual disability is usually considerable. In the authors' experience it is rare for families of these survivors, with the benefit of hindsight, to feel that the decision to proceed with surgery was the right one.

## QUESTION 5: WHEN SHOULD ELEVATED BLOOD PRESSURE BE LOWERED IN THE ACUTE STAGE?

There is no good trial evidence to guide blood pressure (BP) management in the acute stage. Just as with BP lowering in the acute phase of cerebral infarction, the balance of the risks and benefits is unknown. The concern in ICH is that a high BP will result in expansion of a haematoma (Ohwaki et al, 2004). On the other hand, patients with chronic hypertension and disturbed cerebral

*Figures 3(a–c). Arteriovenous malformation right occipital lobe in a pregnant woman who presented with visual field loss. 3a. Magnetic resonance image (MRI) T1 weighted image; 3b. MRI T2 weighted image; 3c. Magnetic resonance angiography.*



autoregulation may need higher BPs to maintain cerebral perfusion. The American Heart Association guidelines recommend BP lowering if the mean arterial pressure reaches 130 mmHg or more (Broderick et al, 1999). In practice, this means keeping the BP below about 170/110 mmHg. The choice of oral *vs* intravenous agents for BP lowering depends somewhat on the level of the BP elevation and the clinical state of the patient. Most patients can be managed with an oral agent or a nitrate patch if unable to swallow. Small doses, repeated if necessary, are preferred.

## QUESTION 6: WHAT SHOULD BE DONE IF A PATIENT WITH SPONTANEOUS ICH DEVELOPS A DEEP VENOUS THROMBOSIS OR PULMONARY EMBOLISM WHILE IN HOSPITAL?

This situation is not uncommon, especially during rehabilitation. The management of proximal DVT or PE in people with acute cerebral infarction usually involves anticoagulation with heparin or heparinoid, followed by oral vitamin K antagonists such as warfarin. In the context of recent ICH, this decision is complicated by the risk of expansion of the haematoma or recurrent ICH during anticoagulant therapy and needs to be balanced against the risk of a fatal outcome from untreated (or undertreated) DVT and PE.

The estimated risk of recurrent ICH in someone anticoagulated for 3 months is 3–5% (Hart, 2004), with the risk highest in the first 2 weeks following ICH. Against this must be balanced an estimated risk of fatal PE of 25% for someone with proximal DVT or PE without anticoagulation (Barritt and Jordan, 1960). This figure comes from a trial published in 1960 as there are no more recent trials that include an untreated group. However, experience from prophylactic anticoagulation trials in patients undergoing orthopaedic surgery, where there is a high rate of DVT, but low perioperative mortality, suggests that the risk of fatal PE in people not anticoagulated may not be as high as 25%.

Some authorities recommend a filter in the vena cava in this situation, generally without anticoagulation. Although effective, caval filters are associated with complications, particularly new DVT. Newer caval filters do not need to be placed permanently. An attractive option for people with early proximal DVT after ICH would be placement of a removable filter. The filter could be kept in place for 2–4 weeks, where the risk of rebleed is highest with warfarin, followed by removal of the filter and treatment with warfarin for 2 months. For people with ICH and proximal DVT occurring more than 3 weeks from ICH, treatment with heparin or heparinoid followed by warfarin for 3 months (target INR = 2.0–3.0) is a reasonable strategy. Clearly, when the risk of fatal PE is much lower, for example, when there is a DVT distal to the knee, anticoagulation could be withheld altogether. Given the risks involved, it is important to include the patient and his/her family in decision making and to document this.

## QUESTION 7: SHOULD ASPIRIN BE GIVEN AS SECONDARY VASCULAR PREVENTION IN A PATIENT WITH SPONTANEOUS ICH AND PREVIOUS CEREBRAL OR MYOCARDIAL INFARCTION?

In general, the answer is 'no'. Aspirin increases the risk of recurrent ICH by approximately 40%, an absolute increase of 0.8% per year (Hart, 2004). In most situations, the relative benefits of antiplatelet agents such as aspirin for preventing recurrent ischaemic vascular events are outweighed by the increased risks of recurrent bleeding in someone taking aspirin.

In particular, the authors would almost always avoid any antiplatelet agents for people with ICH resulting from previous aspirin use or suspected cerebral amyloid angiopathy (e.g. older patients with lobar haemorrhages or with MRI evidence of multiple microbleeds) as there is a higher risk of recurrent haemorrhage in these groups (see Question 10). The situations where aspirin may be considered for a number of types of patients who were not taking aspirin at the time of their ICH and who have a deep ICH, thought to be secondary to hypertension are summarized in *Table 2*.

## QUESTION 8: SHOULD ASPIRIN OR WARFARIN BE USED FOR PRIMARY OR SECONDARY PREVENTION OF ISCHAEMIC VASCULAR EVENTS IN SOMEONE WITH ATRIAL FIBRILLATION AND SPONTANEOUS ICH?

Warfarin increases the risk of new ICH by approximately three times in patients anticoagulated for nonvalvular AF, but the risk of recurrent ICH with continued anticoagulation is likely to be much higher. In a decision analysis using an estimated doubling of ICH recurrence risk with warfarin, the preferred option, in terms of quality of life years (QALYs), for all lobar ICH and most deep ICH was not to anticoagulate the patient unless the annual absolute risk of ischaemic stroke was greater than 7% per year (Eckman et al, 2003).This analysis took account

of the reality that outcomes are worse for ICH than for cerebral infarction.

The risk of recurrent stroke in the first year after an ischaemic stroke in a person with AF without anticoagulation may be as high as 15%, falling to about 5% per year thereafter (Saxena and Koudstaal, 2004). Given that the estimate of ICH recurrence on warfarin in Eckman et al (2003) may understate the true position, few patients with ICH and AF justify anticoagulation. Any decision should be discussed with the patient and his/her family because of the risks involved. Aspirin is associated with lower ICH recurrence rates than warfarin but is also associated with lower effectiveness in preventing ischaemic strokes in people with AF. The authors believe that for most patients, the balance is in favour of not using aspirin in this situation.

## QUESTION 9: CAN WARFARIN BE RESTARTED IN SOMEONE WITH A PROSTHETIC HEART VALVE WHO HAS A SPONTANEOUS ICH? IF SO, WHEN?

The risks of new ischaemic events in someone with an artificial heart valve, not taking anticoagulant therapy, vary depending on the type of device; a mechanical valve has a greater risk of thromboembolism than a tissue valve. However, the risk is considerable and expert advice should be sought. The little evidence available suggests that it is safe to withhold anticoagulation for up to 10–21 days following ICH in a person with a mechanical valve (Widjicks et al, 1998; Phan et al, 2000)

The difficulty arises when deciding whether or not to restart anticoagulant therapy. The balance of potential benefits and risks needs to be assessed in each patient. There has been one published series of patients with prosthetic heart valves where anticoagulation was re-instituted after ICH. This study showed that the rate of recurrent ICH was low but most participants also had lower intensity anticoagulation than previously, and this may have been associated with an increased risk of new ischaemic events (Butler and Tait, 1998).

A commonsense approach needs to be taken in any individual patient. It may not be appropriate to re-institute anticoagulation in someone with severe disability requiring long-term nursing-home care. In contrast, it may be safe to re-start anticoagulation in a patient with ICH associated with a markedly elevated INR with the aim of keeping the INR in the therapeutic range.

The authors would re-institute anticoagulation in most patients with mechanical heart valves and ICH, especially those with a typical hypertensive basal ganglia ICH and good recovery. The authors would usually wait at least 10–14 days before reinstituting anticoagulation and would aim for an INR of 2.5–3.5.

## QUESTION 10: WHAT SHOULD THE PATIENT WITH NO UNDERLYING STRUCTURAL LESION BE TOLD ABOUT THE RISK OF HAVING ANOTHER ICH?

The risk of recurrent ICH depends on the 'type' of ICH. Patients with deep hemispheric 'hypertensive' bleeds have a recurrence rate of 2–3%

**TABLE 2.**
**Use of asprin for secondary prevention of vascular events in patients with deep intracerebral haemorrhage (ICH) considered secondary to hypertension**

| Presentation | Comments* | Recommendations |
|---|---|---|
| First month after myocardial infarction (MI) | 3.6% absolute benefit all vascular events, of which 2.4% is a mortality benefit (Hennekens, 2004) | Aspirin recommended, but caution needed if very early after ICH (<2 weeks) |
| Previous, but not very recent MI | 3.8% absolute benefit all vascular events over 27 months (Hennekens, 2004) with i.e. annual benefit of around 1.7%. Marginal net benefit over increased rebleed rate woth asprin | Aspirin not recommended |
| Previous Transient ischaemic attack or cerebral infarction | 3.6% absolute benefit over 29 months (Hennekens, 2004) giving the same equation as for previous item | Aspirin not recommended |
| Very recent TIA or minor cerebral infarction | This is influenced by information documenting a very high early recurrence rate (Coull et al, 2004), which would translate into an approximate 3% absolute benefit of aspirin in the first 3 months following TIA or minor cerebral infarction | Use of aspirin supportable, but more information on early risk required before use can be recommended |
| Acute cerebral infarction | 0.9% absolute benefit for death and dependency at 6 months (Hennekens, 2004) | Aspirin not recommended |

* Assumes 0.8% annual increase in ICH rebleed rate with asprin

per year (Bailey et al, 2001). In those with lobar haemorrhages, the rate of recurrent ICH may be as high as 28% over 20 months (Greenberg et al, 2004). The presence and number of 'microbleeds' on MRI scanning in those with lobar haemorrhage correlates with increasing probability of recurrent ICH, and may be used in the future to stratify the risk of re-bleeding and guide treatment decisions in individual patients.

## CONCLUSIONS

This article provides some management suggestions for patients with ICH. The authors acknowledge that there is room for disagreement with many of their suggestions and welcome feedback. ICH is sufficiently common and serious that some of the questions raised above should be investigated with appropriate randomized trials so that clinicians can make evidence-based decisions that are likely to lead to better outcomes for their patients. HM

*Conflict of interest: none*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## KEY POINTS

- Spontaneous intracerebral haemorrhage (ICH) is a reasonably common cause of stroke that poses many difficult challenges to hospital doctors.
- There is little robust trial evidence to support most interventions in patients with spontaneous ICH.
- Aspirin is generally not recommended for the secondary prevention of vascular events in patients with previous ICH.
- Warfarin is generally not recommended for secondary prevention of vascular events in people with atrial fibrillation who have had a spontaneous ICH.
- Warfarin can be safely withheld for 10–21 days and reinstituted in most patients with prosthetic heart valves who have a spontaneous ICH.
- Lobar haemorrhage in elderly patients is associated with a higher risk of rebleed than deep haemorrhages and particular caution with the use of antiplatelet or anticoagulant medication is warranted.


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