

# Intracerebral Haemorrhage

## Introduction

Spontaneous intracerebral haemorrhage carries a higher mortality and poorer functional outcome than ischaemic stroke or subarachnoid haemorrhage.<sup>1</sup> The mortality at one month from intracerebral haemorrhage has been observed to range from 35% – 52%. After six months, only 20% of patients can be expected to be independent. The incidence varies between different populations (15 – 35 per 100,000) but is generally twice that of subarachnoid haemorrhage. Despite the damaging impact of this condition, even the basic surgical and medical management varies widely between centres with no good evidence base for best practice. Intracerebral haemorrhage has been recently targeted as a high priority for further clinical stroke research and there have been some recent advances in understanding this condition, and towards improving outcome in the future. In particular, the results of the STICH trial (International Surgical Trial in Intra-Cerebral Haemorrhage) which randomised 1033 patients between early surgery and initial conservative therapy have recently been published;<sup>2</sup> and new avenues of early treatment to prevent clot expansion using activated factor VII show promise.<sup>3</sup>

## Differential diagnosis

Table 1 outlines the different causes of intracerebral haemorrhage. The majority of intracerebral haemorrhage (70 – 80%) is termed primary in nature and results from chronic small vessel disease processes such as intraparenchymal hypertensive small vessel microaneurysms or amyloid angiopathy. Secondary intracerebral haemorrhage can be due to a structural lesion (e.g. tumour, arteriovenous malformation, intracranial berry aneurysm), bleeding diathesis (e.g. warfarin, aspirin, alcohol induced coagulopathy), or a disease process causing acute and severe hypertensive changes such as abuse of sympathomimetic drugs (cocaine, ecstasy, amphetamines) or eclampsia in pregnancy (Figures 1a and 1b).

It is important to note that at a practical level, the distinction between differential causes of intracerebral haemorrhage is not always clear cut e.g. microaneurysmal

small vessel changes can occur (with increasing prevalence in older patients) in the absence of clinical hypertension; an alcohol induced coagulopathy may exacerbate a bleed from other causes such as amyloid angiopathy. Secondary intracerebral haemorrhage can also occur into an ischaemic cerebral infarct. This latter entity will become more frequent with the advent of widespread use of acute thrombolysis for reperfusion in ischaemic stroke.

## Clinical presentation and radiological assessment

Important clinical points to note are: -

1. Any features of trauma that may confound the diagnosis of a spontaneous haemorrhage.
2. The presence of co-morbidity that may predispose to intracerebral haemorrhage (e.g. hypertension, anticoagulant history, use of illicit drugs or alcohol, and haematological disorders).
3. Any recent history of headache, focal deficit or seizures that may indicate the presence of an underlying cerebral lesion.
4. The presence of focal neurological deficit and the level of consciousness as assessed objectively with a breakdown of the Glasgow Coma Score.

Intracerebral haemorrhage classically presents with a sudden onset neurological deficit and features of raised intracranial pressure including headache, vomiting and markedly elevated blood pressure, whereas ischaemic stroke is more likely to present with a sudden onset deficit alone. Early progression of neurological symptoms including deterioration in the level of consciousness within the first few hours is more common for intracerebral haemorrhage (over 50%) than for ischaemic stroke or subarachnoid haemorrhage (5% - 20%).<sup>1</sup> This is thought to be due to the presence of early continued bleeding and hence clot expansion, during the evolution of an intracerebral haematoma.

These clinical features may be helpful in indicating which patients presenting with a sudden onset neurological deficit are likely to have suffered an intracerebral haemorrhage, but they cannot be reliably used to differentiate ischaemic stroke from haematoma. Hence emergent, rapid access CT scanning is essential in the diagno-



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**Table 1: Causes of Spontaneous Intracerebral Haemorrhage**

<b>Primary</b> <i>Chronic hypertension</i> <i>Amyloid angiopathy</i>
<b>Secondary to Structural abnormality</b> <i>Aneurysm</i> <i>Arteriovenous malformation (AVM)</i> <i>Dural arteriovenous fistula</i> <i>Cavernous haemangioma</i> <i>Tumour</i> <i>Haemorrhage into ischaemic cerebral infarct</i> <i>Moya moya disease</i> <i>Sagittal sinus thrombosis</i> <i>Vasculitis/inflammatory vasculopathy</i>
<b>Secondary to coagulopathy</b> <i>Iatrogenic (warfarin, aspirin, thrombolysis)</i> <i>Alcohol induced coagulopathy</i> <i>Blood dyscrasias e.g leukaemia, thrombocytopenia,</i> <i>Hepatic failure, renal failure</i>
<b>Secondary to severe acute hypertension</b> <i>Sympathomimetic drugs</i> <i>(cocaine, ecstasy, amphetamines)</i> <i>Pregnancy - eclampsia</i>

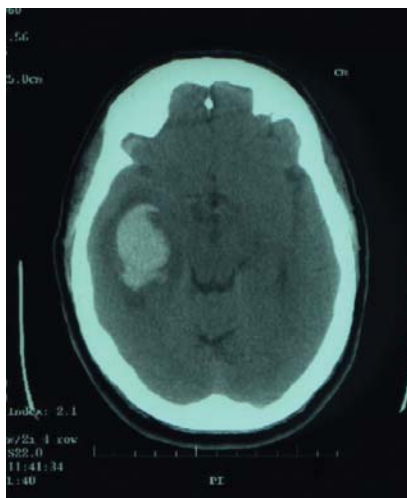


Figure 1a: Presentation CT scan of a 68 year old patient with sudden onset left/right agnosia and symptoms of raised intracranial pressure. An intracerebral haemorrhage was identified in the right temporal region causing mass effect. He improved without haematoma evacuation.

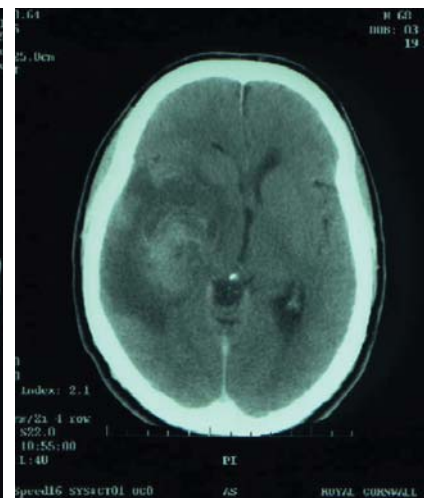


Figure 1b: Five weeks later he developed symptoms of raised intracranial pressure. A repeat CT scan revealed a space-occupying lesion, confirmed at biopsy to be a glioblastoma multiforme.

sis and subsequent management. It allows assessment of the size and location of haemorrhage along with the features of mass effect such as the degree of midline shift and effacement of the basal cisterns indicating pending tentorial herniation. The presence of intraventricular haemorrhage with resultant hydrocephalus is also important in determining surgical treatment. CT will often give information of underlying lesions causing secondary haemorrhage. Aneurysmal haemorrhage is usually associated with the presence of subarachnoid blood and typical bleed patterns extending to the Sylvian fissure (for middle cerebral artery aneurysms) or paramedian frontal lobe haemorrhage extending to the interhemispheric fissure anteriorly (for anterior communicating artery or pericallosal artery aneurysms). Arteriovenous malformations will usually show calcified vessels in association with the AVM. Tumours may be suspected where there appears to be a separate mass adjacent to the acute intracerebral haematoma (usually with contrast enhancement) or a degree of surrounding cerebral oedema in excess to that expected for an acute haematoma. Malignant melanoma is the most common metastasis to present with intracerebral haemorrhage and high-grade intrinsic gliomas can infrequently present with haemorrhage (Figures 1a and 1b). Intracerebral haemorrhage secondary to sagittal sinus thrombosis is often bilateral, paramedian in location and associated with cerebral oedema arising from cerebral venous congestion. Following intravenous contrast, the 'empty delta' sign may be evident in the superior sagittal sinus.

Lobar, peripherally located haemorrhage in the elderly is often attributed to amyloid angiopathy. More centrally located haemorrhage originating in the putamen, globus pallidus, thalamus, or internal capsule is classically assigned to chronic hypertension (as is haemorrhage in the pons and cerebellum). However these assumptions can frequently be incorrect. In a study of 102 patients<sup>4</sup> with intracerebral haemorrhage, 58 patients had no CT features of an underlying structural lesion (the presence of subarachnoid, Sylvian fissure or intraventricular haemorrhage, abnormal intracranial calcification, prominent vascular structures). Of these, 42 underwent delayed cerebral angiography revealing 10 unsuspected vascular lesions (8 AVM's and 2 aneurysms). More recently, the high sensitivity of an MRI or CT scan with contrast once the haemorrhage is resolving (usually 4-6 weeks after the bleed) should resolve the need for conventional invasive cerebral angiography to exclude a vascular lesion such as an AVM. Angiography can then be confined to those patients with abnormal findings indicative of an AVM or aneurysm.

### Initial medical treatment

The initial medical treatment is supportive. Patients suffering from intracerebral haemorrhage frequently show respiratory or cardiovascular instability and hence airway, breathing and circulation are the first priorities, even in a patient demonstrating significant neurological decline. Ventilation will be required in patients

with a Glasgow Coma Score of less than 8, if the airway or oxygenation is not being maintained, and in patients who are agitated or combative to the point that a CT scan cannot be performed. Ventilation may also be needed for patients suffering repeated or prolonged seizures. Aspiration of gastric contents whilst the airway is unprotected is a frequent risk in patients who are showing significant neurological decline.

Blood pressure management is a controversial issue.<sup>1</sup> Patients often have a history of chronic hypertension and will therefore require higher than normal mean arterial blood pressures to maintain adequate cerebral perfusion. In the presence of a large intracerebral haematoma, intracranial pressure may be significantly raised and hence require a higher than normal arterial blood pressure in order to maintain an adequate cerebral perfusion pressure. Yet there is evidence that those patients with abnormally elevated blood pressures are more likely to deteriorate clinically within the first few hours because of ongoing bleeding causing haematoma enlargement.<sup>5</sup> There is a lack of good evidence regarding the best blood pressure management strategy to employ, and it may be beneficial to individualise blood pressure targets depending on the patient's clinical circumstances. Recommendations have been made by the Stroke Council, American Heart Association<sup>1</sup> that patients with chronic hypertension should have mean arterial blood pressures not exceeding 130mm Hg, that if systolic arterial blood pressure falls below 90mm Hg then pressors should be given, and where intracranial pressure monitoring is used, CPP should be maintained at greater than 70mm Hg.

In patients who are warfarinised, this should be reversed immediately and fully using fresh frozen plasma and vitamin K. The risk of extension of the intracerebral haematoma remains very high whilst anticoagulation is not reversed, whereas the risk of an adverse thromboembolic event even in those patients who are most at risk (e.g. with a metal prosthetic heart valve replacement) is minimal within the first week.

A significant proportion of patients experience ongoing haemorrhage within the first few hours causing intracerebral haematoma expansion and thus clinical deterioration. A recently published randomised controlled trial has shown improved survival and functional outcome from the early administration of activated Factor VII to prevent haematoma propagation.<sup>3</sup> This trial is significant in being the only medical treatment to show a clinical improvement in outcome for intracerebral haematoma. Practically, there will be difficulties in the widespread institution of this type of treatment because patients must be treated very early in the evolution of their intracerebral haematoma and because of the present prohibitive cost of treatment with activated Factor VII.

### Surgical treatment of intracerebral haemorrhage

Surgical treatment of intracerebral haemorrhage

includes intracranial pressure monitoring for guiding subsequent intensive care management, ventricular drainage for the relief of hydrocephalus, and partial or complete evacuation of the intracerebral haematoma. The latter can be achieved by open craniotomy or by less invasive procedures such as stereotactically guided burr hole aspiration and endoscopically guided aspiration. In addition, a thrombolytic agent such as the plasminogen activator, urokinase can be instilled into the haematoma cavity to aid clearance of the clot.

The rationale for haematoma evacuation is potentially twofold. Firstly it is effective in relief of raised intracranial pressure when there is significant mass effect. This may improve outcome by preventing brainstem compression and subsequent coning, improving global cerebral perfusion to prevent ongoing ischaemia to the brain, or indirectly by allowing control of intracranial pressure so that patients can be more rapidly weaned on the intensive care unit and hence be less susceptible to medical complications such as ventilator associated pneumonia. Secondly haematoma evacuation may be beneficial in minimising the surrounding brain oedema and secondary neurotoxic injury that occurs as a delayed reaction within the penumbra surrounding the intracerebral blood clot.<sup>6</sup> The early retraction of blood clot, the presence of thrombin and activation of the coagulation cascade, and the presence of haemoglobin breakdown products is believed to be key in the development of cerebral oedema and secondary neurotoxicity. Balanced against these potential benefits is the added cerebral trauma of surgical evacuation. Evacuation is often only partial and this may not be sufficient to prevent secondary neurotoxicity. Evacuation is more likely to be incomplete (or even leave significant residual haematoma causing mass effect) when less surgically invasive procedures such as endoscopic or stereotactic aspiration are employed. The majority of large intracerebral haemorrhages destroy the internal capsule and hence patients are likely to remain densely hemiplegic. Surgical evacuation of a haematoma large enough to cause significant mass effect may therefore achieve little more than to convert patients who would not survive into patients who will be left severely disabled.

McKissock *et al.* published the first randomised controlled trial for the surgical treatment of intracerebral haemorrhage in 1961,<sup>7</sup> showing that outcome was worse in surgically as opposed to conservatively treated patients. Subsequent trials have generally shown conflicting results with insufficient power. To progress from this, the STICH trial<sup>3</sup> recruited 1033 patients who were randomised to early surgery or initial conservative therapy. Patients were eligible if they presented within 72 hours of a supratentorial, non aneurysmal, non AVM bleed, if the treating neurosurgeon was uncertain which treatment was better for the patient (the clinical uncertainty principle) and if surgical treatment was intended within 24 hours. This was a trial for early surgery and so patients in the medical arm could undergo haematoma evacuation at a later date (about a

quarter of patients did require this). Outcome and mortality did not differ significantly between the two groups. Predefined subgroup analysis showed benefit in early surgery when the haematoma was less than 1cm from the cortical surface, suggesting that surgery might be better when less surgical trauma is caused in reaching the haematoma, a possibility which has previously been raised from the benefit conferred in outcome from endoscopic evacuation of intracerebral haematoma in an earlier trial.<sup>8</sup> One very important finding of STICH was that patients presenting with a Glasgow Coma Score of eight or less had an almost universally poor outcome.

**Summary**

Intracerebral haemorrhage remains a frequent and devastating condition within the central nervous system. The evidence base for considering optimal treatment is lacking but recent trials are beginning to rectify this. Progress in improving outcome for the future will require widespread availability of good quality neuro-intensive care facilities and early referral systems for acute stroke in general. In addition a

better understanding of the factors that produce early clinical deterioration by haematoma enlargement (and particularly how this can be controlled haematologically and with blood pressure management), and delayed deterioration by secondary neurotoxic processes will be important. Any future trials of surgery are likely to need to consider techniques that minimise trauma to the brain, yet achieve consistently good haematoma evacuation.

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