to true, established hypertension and not to the transient hypertension caused by the hæmorrhage, so often seen in an ordinarily normotensive patient.

(2) *Angiomas*
The second major group is that of arteriovenous malformations which have bled. Although commonly referred to as angiomas, they are not, of course, neoplasms. They vary from minute groups of abnormal capillary-like vessels, too small to be demonstrated by angiograms, to huge masses involving most of a cerebral hemisphere. Prognosis for recurrent bleeding is not so grave as with aneurysms; some never bleed more than once, others may go for many years between bleeds. Some are technically accessible and operable; others are not. It is widely agreed that, if it is possible and safe, an angioma which has bled should be excised. Radiotherapy has been and is used, but despite some ambitious claims most of us consider it of little or no value. Newer and experimental techniques are being tried, such as cryogenic obliteration and injection of plastic beads into the abnormal vessels to induce thrombosis, but they are not yet evaluated.

(3) *Primary Intracerebral Hæmorrhage*
Finally there is the problem of the 'stroke' – the primary intracerebral hæmorrhage. In 1960 the author of an editorial in the *Lancet* wrote on the subject of 'Cerebral Apoplexy': 'In this common condition, what is the mortality rate? Statistics of conservatively treated cases are confined to reports of cases verified by necropsy; it is hardly surprising that the mortality rate of cases treated conservatively is then discovered to be one hundred per cent' (*Lancet*, 1960, ii, 32).

We have learned a great deal since then, notably that the middle-aged, hypertensive female tolerates her stroke as remarkably well as she tolerates hypertension. In the great stroke trial carried out at the Atkinson Morley Hospital, in which I was deeply involved (McKissock *et al.* 1961), these women had a conservative mortality of only 30%. This figure was disastrously doubled by careful craniotomies for evacuation of the clot.

It is a fair generalization that surgical evacuation of hæmatomas does more harm than good. Nevertheless there are exceptions, and I think most neurosurgeons would agree that a large hæmatoma in a relatively alert patient with severe neurological signs should be removed, as should the occasional hæmatomas that behave like chronic space-occupying lesions and produce papillœdema.

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Cerebral Arterial Reactivity and Spasm After Subarachnoid Hæmorrhage

It is generally agreed that extreme vasoconstriction, usually known as 'spasm', affects a proportion of patients after subarachnoid hæmorrhage and that this spasm is sometimes responsible for severe cerebral ischæmic changes (Pool & Potts 1965, Fletcher *et al.* 1959, Alcock & Drake 1965). Consequently it may be desirable to attempt to relieve it in certain cases, but first it is necessary to understand the nature of spasm.

Our aims in this work have therefore been: (1) to establish a radiological technique which would provide accurate measurements of cerebral arteries of baboons down to an internal diameter of the order of 0·5 mm and to make these measurements in a 'blind' way so that they were not influenced by expectation; (2) to determine the normal reactivity of the basal arteries of man and the experimental animals to common physiological stimuli (arterial CO_2 tension, mean systemic arterial blood pressure, central venous pressure, arterial blood pH) so that man and baboon may be compared; and (3) thus to show and explain the significance of small changes in diameter of vessels after subarachnoid hæmorrhage.

Techniques
The technique of angiography under carefully monitored and controlled conditions and the 'blind' techniques of measuring the arteries have been described (du Boulay & Symon 1971). Additional points relevant to the present study are: (1) that transient hypotension has been induced by exhausting air from a small decompression chamber into which the lower half of the monkey's body has been introduced; (2) that 'subarachnoid hæmorrhage' has been reproduced by injecting 2 ml arterial blood (drawn freshly from the aorta of the monkey through the femoral pressure-monitoring catheter) into the cisterna magna. The injection has been slow, taking 8–10 seconds, and has been made through a needle introduced only for this purpose and then withdrawn.

FINDINGS

Normal Reactivity
(1) *To $Paco_2$ changes:* By measuring the diameters of the major vessels at the brain's base shown by angiography under carefully monitored conditions, data have been obtained about the

reactions of these vessels to $Paco_2$ and systemic blood pressure changes.

Most of the findings concerning reactivity of human and baboon arteries to $Paco_2$ alteration were presented by du Boulay & Symon (1971). In brief, basal arteries, like cortical pial vessels, dilated as $Paco_2$ rose in and above the normal range. The arteries were narrowest, however, when $Paco_2$ was just below the lower limit of normal range, at about 30 mmHg. A fall in $Paco_2$ levels from about 28 mmHg resulted in vasodilatation rather than vasoconstriction.

(2) *To changes in arterial blood pressure:* Before making any deductions about the behaviour of spastic arteries, we considered it essential also to know how basal arteries respond to alterations in blood pressure alone.

It is well known that a moderate fall in systemic blood pressure results immediately in dilatation of the small cortical pial arteries (Fog 1937). Angiographically, in our experiments, some of the smallest vessels for which measurement is possible (branches of the middle and anterior cerebral arteries of about 0·8 mm diameter) are seen to behave in this way. Our recent studies have shown, however, that the larger vessels do not.

In these particular experiments on blood pressure the main trunk of the middle cerebral artery was rarely well visualized and the middle cerebral branches which could be measured were generally less than 1·0 mm in diameter. Since there was some evidence that the arteries of this small size tended to react in an opposite way to the larger vessels, calculations have been made from the measurements of the carotid and anterior cerebral arteries alone.

In one monkey it was possible to measure portions of both carotids. In the others, measurements have been restricted to one side. It was shown that these larger vessels were all behaving in the same way and thus it has been thought justifiable to treat the trunks and main branches of the circle of Willis of a single monkey as a whole. By adding the diameters of the vessels measured and comparing this figure with the added diameters measured at identical points in the same monkey under different conditions of blood pressure a statistical evaluation of vasoconstriction may be obtained. This comparison gives a 'percentage vasoconstriction' for each experiment which represents the vasoconstriction of that portion of the vascular tree considered as a whole.

It has been shown that there is a striking difference between experiments in which the arterial blood pressure is dropped by a mean of 29 mmHg or more and those in which the blood pressure fall is less than this.

In Group 1 in six experiments on 3 monkeys, the mean fall in blood pressure was less than 29 mmHg. Mean vasoconstriction was 1·2% ($\pm$ 0·26) by comparison with the summed diameters of the same vessels under control conditions ($P<0·001$). In Group 2 in five experiments on 2 monkeys, the mean fall in blood pressure was 29 mmHg or more. Mean vasoconstriction was 6·7% ($\pm$ 2·55) by comparison with the summed diameters of the same vessels under control conditions ($P<0·01$). (One monkey took part in both types of experiment.) The difference between these two groups is significant ($P<0·01$).

Thus a drop in blood pressure, caused by subjecting the lower half of the body to decompression, results in immediate arterial vasoconstriction of the intracranial carotid and main trunks of anterior cerebral arteries. (The extracranial courses of internal carotid and vertebral arteries and at least one branch of the external carotid were shown to behave in a similar fashion.)

An angiogram obtained within seconds of the beginning of the fall in blood pressure demonstrates the rapidity of the reaction. It seems, therefore, that these larger intracranial arteries all take part in the body's general reaction to acute hypotension and thus behave not as cerebral but as systemic vessels. It is interesting to observe that the part of the intracranial vascular tree which responds in this way to severe falls in blood pressure is much the same as the part which tends to be affected by spasm after subarachnoid hæmorrhage and that the region also corresponds more or less closely with the major distribution of catecholamine-containing nerve fibres which may be demonstrated by the fluorescent technique of Falck & Owman (1965).

The Time-course of Spasm

The changes in diameter of basal arteries, which we now know accompany alterations in physiological factors such as may occur during an experimental procedure, are of the same order of magnitude as milder degrees of arterial spasm. Consequently it is essential both to monitor and to control blood pressure and $Paco_2$ during spasm experiments. After an initial angiogram by the technique previously described, we have slowly injected 2 ml freshly drawn arterial blood into the cisterna magna by needle puncture.

Further angiograms have been performed at intervals of five to thirty minutes for up to 2½ hours, and again a week later before and after the introduction of a further 2 ml fresh blood, and in some animals at weekly intervals thereafter. Nineteen experiments have been performed.

Spasm of the internal carotid artery and some of its branches is often seen by the naked eye

about 20 minutes after the cisternal injection and is revealed by measurement of arteries after only 5 minutes. It increases in severity for ½ to 1 hour. Sometimes it begins to diminish after 1½ hours. Details of the time-course are to be published later.

The Reactivity of Spastic Arteries

In baboons in the present series the CO_2 tension has been altered after an initial angiogram by adding CO_2 to the inspired gases; then, after another angiogram, the CO_2 has been turned off and further angiography has been delayed until $Paco_2$ has fallen again by a substantial amount. The blood pressure has been monitored but not controlled. Changes in the diameters of the spastic arteries have regularly been observed to accompany the alterations in $Paco_2$ and the continuing reactivity of these arteries during the first hour of spasm has been substantiated.

An intriguing problem has, however, been the confirmation that a rise in $Paco_2$ does not always cause vasodilatation, but may sometimes be accompanied by vasoconstriction. All the experiments have been conducted within the normal and supranormal range of $Paco_2$, and the onset of peripheral tissue hypoxia does not seem a very likely explanation for the observed reactions which have consistently followed a certain pattern. This pattern may be summarized as (1) probably a persisting normal reactivity to CO_2, and (2) an enhanced response to another factor, to be described in a further paper.

In general terms two possible explanations present themselves. These are (1) that the arteries are possibly changing passively in response to blood pressure alterations (in other words that both sides of the presumed autonomic pathways have been blocked and tone abolished), or (2) that only one side of the presumed autonomic control is at fault.

Recent work by Fraser *et al.* (1970) has tended to incriminate the α-adrenergic receptors. If more than one fraction of blood is involved experimentation, already difficult because of the lack of information about normal reactivity of basal arteries, becomes doubly so.

Our present findings seem to provide some support for a theory of spasm which includes interference with the neurogenic control of these vessels. The experimental findings do not, however, necessarily incriminate the α-receptors as being the site of the essential primary lesion.

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Management of the Acute Completed Major Stroke

Once the diagnosis of a completed major stroke has been established it is not unusual for a sense of mild depression to affect the physician concerned because, however optimistic one's outlook, it is likely that recovery, if it occurs at all, will be incomplete and of poor quality. Strokes may be due to infarction or hæmorrhage and, although in many patients the differentiation is easy, in some it is clinically impossible to distinguish between an infarct and a small intracerebral hæmatoma. Similarly, in unconscious patients with blood-stained cerebrospinal fluid it may be difficult to decide for a day or two whether the bleeding began in the brain and ruptured into the subarachnoid space or *vice versa*, and even whether its origin was supra- or sub-tentorial. Since the level and duration of coma is the major prognostic factor for survival it seems sensible when considering treatment to divide patients into comatose and non-comatose groups (Table 1). I shall exclude as far as possible primary subarachnoid hæmorrhage due to rupture of an aneurysm or angioma because I think such patients are eventually a surgical problem, although their immediate treatment may be that of any unconscious patient.

Comatose Patients

Most of these are patients who have suffered a cerebral hæmorrhage and more than half have blood-stained cerebrospinal fluid; a few are unconscious from a large cerebral infarction and others may have a contained or expanding intracranial hæmatoma with normal CSF. Treatment is at first the general management used for un-

Table 1
Relationship of mortality to length of coma in 500 consecutive stroke admissions 1965–70

Length of coma	*No. of patients*	*Mortality at 4 weeks*
Conscious on admission	298	12%
Less than 24 hours	70	45%
Less than 48 hours	62	85%
More than 48 hours	70	98%