The Effect of a Simulated Subarachnoid Hemorrhage on Cerebral Blood Flow in the Monkey

BY ALBERT N. MARTINS, M.D., THOMAS F. DOYLE, B.S., NORWYN NEWBY, M.D., ARTHUR I. KOBIRNE, M.D., AND ARCHIMEDES RAMIREZ, M.D.

Abstract: The hydrogen clearance method was used to measure local and total cerebral blood flow (CBF) in the rhesus monkey before and for five hours after a simulated subarachnoid hemorrhage (SAH). CBF remained stable after SAH unless SAH was associated with a fall in cerebral perfusion pressure. In addition, cerebrovascular resistance did not increase after SAH. These results suggest that vasoactive agents in fresh whole blood, and the arterial spasm they produce when added to cerebrospinal fluid (CSF), play only a limited role in the pathogenesis of ischemic encephalopathy that follows an SAH.

Additional Key Words: cerebrovascular resistance, hydrogen clearance, intracranial hypertension, vasospasm

Introduction

Patients who do not die immediately following rupture of an intracranial berry aneurysm and the attendant subarachnoid hemorrhage (SAH) all too often die days or weeks later to a poorly understood progressive encephalopathy.1 Most authors agree that if either hematoma or hydrocephalus is not present, the underlying process in the evolution of encephalopathy following SAH is one of ischemia1-11 progressing to brain infarction.12-15 Precisely how this comes about is uncertain, but out of the controversy emerges one clear consensus: arteries of the mammalian brain constrict shortly after autologous whole blood contacts their cerebrospinal fluid-bathed adventitial surfaces.14-30 Proceeding from this observation, many authorities have proposed that vasoactive agents in blood and the arterial spasm they produce play an important, if not the principal, role in the development of ischemic encephalopathy after an SAH.31-34 This hypothesis predicts that blood injected into the intracranial subarachnoid space will provoke arterial spasm, increase cerebrovascular resistance (CVR), and thereby reduce cerebral blood flow (CBF).

We tested the hypothesis by using the hydrogen clearance method to measure both total and local CBF in the monkey before and for five hours after a simulated SAH.

Methods

GENERAL

Rhesus monkeys, unselected as to sex and weighing between 3 and 5 kg, were initially anesthetized with ketamine (50 mg) and atropine sulfate (0.5 mg) intramuscularly, and pentobarbital (50 mg) intravenously. After they were intubated endotracheally with a cuffed tube, catheters were placed in the femoral artery and vein to allow monitoring of mean arterial blood pressure (MABP), administration of drugs and sampling of arterial blood for immediate, direct analysis of Pco2, PO2, and pH before and after each cerebral blood flow (CBF) study. Subsequently, the monkeys were positioned sphinx-like in a stereotactic headholder and a 19-gauge needle attached to a polyethylene tube was passed percutaneously into the cisterna magna from which we recorded the intracranial pressure (ICP) continuously. Ventilation was maintained with a small-animal respirator at 40 to 44 respirations per minute. The tidal volume was 40 to 45 cc, and the inspiratory phase of the respiratory cycle was 35% of the total. Anesthesia was maintained by an inspired gas mixture of approximately 70% nitrous oxide and 30% oxygen. Enough CO2 was added to maintain arterial Pco2 between 31 and 35 mm Hg (which is normal for the acclimatized awake monkey in our own published experience as well as in the experience of others37). Pao2 ranged between 135 and 150 mm Hg. After an initial intravenous loading dose of 2 mg of tubocurarine chloride, lactated Ringer's solution with the addition of 0.06 mg per milliliter of tubocurarine chloride was infused intravenously to maintain both fluid balance and muscular paralysis during the entire experiment. A heated pad kept the body temperature (rectal) between 37° and 39°C.

CEREBRAL BLOOD FLOW MEASUREMENT

Both local and total CBF were measured by the hydrogen clearance technique that we have previously described.38-41

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Local tissue CBF was measured with six polarographic electrodes of fine platinum wire supported by glass capillary tubes placed stereotactically into the frontal, parietal and occipital lobes, and into the thalamic, hypothalamic, and reticular areas of the diencephalon (fig. 1). Throughout the investigation we did not change the coordinates for the tissue electrodes. Nevertheless, due to technical difficulties, placement of the electrode tip did vary from brain to brain by as much as 2 mm in any direction and probably accounts for some of the variability we observed in flows recorded from a particular target area in different animals. Tissue electrodes were implanted one to seven days before the experiment and affixed to the skull with dental acrylic. Total CBF was determined by measuring the clearance of hydrogen from blood flowing through the torcular Herophili with a polarographic electrode passed transdurally into the torcular at the time of the experiment. CBF determinations were begun by adding hydrogen (5 to 10 vol %) to the inspired gas mixture for ten minutes, after which it was stopped abruptly. The first 40 seconds of the clearance curves were discarded and the remainder analyzed as we have previously described in detail.8-11

EXPERIMENTAL PROCEDURE

More than two hours elapsed between the injections of ketamine and pentobarbital and the first CBF determination. During this period, preparations were completed and the vital signs and blood gases stabilized. Thereafter, CBF determinations were made each hour for the ensuing seven hours. Animals were allocated to three groups: Group 1: controls, no SAH; Group 2: SAH, ICP normal; and Group 3: SAH, ICP increased.

To simulate an SAH, we drilled a hole 1 mm in diameter through the frontal bone in the midline, 40 mm anterior to the inter-aural line. From this point of entry, a 22-gauge spinal needle was advanced stereotactically through a guide along the midsagittal plane at an angle of 45° to Reid's (infra-orbital-meatal) baseline to a depth of 26 mm beneath the dura. This usually positioned the point of the needle in the prechiasmatic subarachnoid space and provided a means of achieving, with experience, an essentially pure and confluent SAH about 80% of the time. After two serial baseline CBF determinations were completed, 4 ml of blood were withdrawn from the femoral artery and immediately injected by hand into the prechiasmatic subarachnoid space. We kept the ICP of the animals in Group 2 below 20 mm Hg during the injection of blood by adjusting the rate of injection while draining CSF through a needle previously placed in the lumbar subarachnoid space. The CSF of animals in Group 3 was not drained and the ICP was allowed to rise during the injection of blood but it was kept at least 30 mm Hg less than MABP. In all experiments the subarachnoid injection was completed within five minutes. At the conclusion of each experiment the animal was killed with an overdose of pentobarbital; the brain was then removed and examined to determine the location of the injected blood. Data from animals that did not receive an essentially pure SAH were discarded.

Location of tissue electrodes from which local blood flow was determined: (a) occipital lobe, (b) parietal lobe, (c) diencephalic reticular formation (left), thalamus (right), (d) hypothalamus, and (e) frontal lobe.
Results
Arterial Po2, Pco2, and pH remained stable in all animals of each group. Each animal's Pco2 varied less than 2 mm Hg from the mean during the entire experiment. In most animals of Groups 2 and 3, the SAH was extensive and confluent throughout the basal cisterns, sylvian subarachnoid space, and in some cases over the convexities and interhemispheric fissure. Those with lesser amounts of blood persisting in the intracranial subarachnoid space were judged to have had a significant SAH if there were blood and clots in the lumbar CSF. SAH produced in Group 3 was on the average more extensive than that in Group 2.

GROUP 1: CONTROLS
Total CBF and local CBF in most areas increased during the first half of the experiment and decreased slightly toward the end (fig. 2). This was most marked in the reticular and hypothalamic areas of diencephalon. Cerebrovascular resistance

$$\text{CVR} = \frac{\text{MABP} - \text{ICP}}{\text{Total CBF}}$$

changed inversely with CBF (fig. 3, table 1).

GROUP 2: SAH, ICP NORMAL
Total and local CBF and CVR were unaffected by the SAH (figs. 2 and 3). The change observed in these parameters after SAH did not differ significantly from changes observed in serial measurements among the controls (table 2).

GROUP 3: SAH, ICP INCREASED
After SAH, mean ICP increased significantly and remained so. Mean total CBF and mean local CBF in most regions remained below pre-SAH levels (fig. 2). However, two groups of seven monkeys showed a fall in CBF after SAH; the remaining four showed an increase in CBF despite the increasing ICP (fig. 4). In two of three animals in which CBF fell, the MABP also fell to levels lower than pre-SAH levels. After SAH, mean total CVR remained below pre-SAH levels. Most animals in this group developed transient cardiac bradyarrhythmias during the SAH and the MABP briefly increased to 175 mm Hg or more (fig. 5, table 3).

Discussion
After SAH, CBF and CVR did not change as one would expect if vasoactive agents in the blood, and the arterial spasm they produce when added to the CSF, play the principal role in the development of ischemic encephalopathy after an SAH. Although spasmogens presumably were present in high concentration in the CSF admixed with fresh blood during the first five hours after the simulated SAH, CBF remained stable unless the SAH was associated with a fall in cerebral perfusion pressure (MABP-ICP).

These observations are in accord with those of
### TABLE 1

**CBF, MABP, ICP and CVR in Controls (Group 1)**

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total CBF</strong> (N = 5)</td>
<td>40 ± 8.3</td>
<td>56 ± 9.4</td>
<td>60 ± 5.4</td>
<td>66 ± 7.7</td>
<td>62 ± 5.2</td>
<td>61 ± 3.7</td>
<td>58 ± 3.9</td>
</tr>
<tr>
<td><strong>Occipital CBF</strong> (N = 4)</td>
<td>32 ± 6.9</td>
<td>34 ± 5.0</td>
<td>41 ± 7.0</td>
<td>39 ± 7.2</td>
<td>39 ± 7.5</td>
<td>43 ± 9.0</td>
<td>40 ± 7.9</td>
</tr>
<tr>
<td><strong>Parietal CBF</strong> (N = 2)</td>
<td>29 ± 16.0</td>
<td>35 ± 21.0</td>
<td>37 ± 18.0</td>
<td>33 ± 20.0</td>
<td>38 ± 28.0</td>
<td>34 ± 24.0</td>
<td>29 ± 24.0</td>
</tr>
<tr>
<td><strong>Reticular CBF</strong> (N = 5)</td>
<td>43 ± 8.5</td>
<td>50 ± 9.7</td>
<td>67 ± 15.0</td>
<td>77 ± 11.0†</td>
<td>75 ± 11.0†</td>
<td>75 ± 7.1†</td>
<td>70 ± 9.2†</td>
</tr>
<tr>
<td><strong>Thalamic CBF</strong> (N = 4)</td>
<td>41 ± 9.4</td>
<td>47 ± 12.0</td>
<td>53 ± 7.2</td>
<td>57 ± 6.0</td>
<td>57 ± 8.4</td>
<td>54 ± 5.2</td>
<td>52 ± 7.3</td>
</tr>
<tr>
<td><strong>Hypothalamic CBF</strong> (N = 4)</td>
<td>25 ± 9.7</td>
<td>45 ± 12.0</td>
<td>52 ± 13.0</td>
<td>57 ± 9.9</td>
<td>63 ± 16.0</td>
<td>64 ± 18.0</td>
<td>64 ± 20.0</td>
</tr>
<tr>
<td><strong>Frontal CBF</strong> (N = 3)</td>
<td>52 ± 20.0</td>
<td>51 ± 15.0</td>
<td>61 ± 24.0</td>
<td>84 ± 39.0</td>
<td>56 ± 15.0</td>
<td>70 ± 23.0</td>
<td>68 ± 27.0</td>
</tr>
<tr>
<td><strong>MABP (mm Hg)</strong> (N = 5)</td>
<td>115 ± 6.0</td>
<td>115 ± 5.0</td>
<td>111 ± 8.0</td>
<td>110 ± 10.0</td>
<td>106 ± 9.0</td>
<td>98 ± 7.0</td>
<td>114 ± 11.0</td>
</tr>
<tr>
<td><strong>ICP (mm Hg)</strong> (N = 5)</td>
<td>8 ± 2.0</td>
<td>8 ± 1.0</td>
<td>7 ± 2.0</td>
<td>5 ± 2.0</td>
<td>6 ± 1.0</td>
<td>4 ± 1.0</td>
<td>5 ± 1.0</td>
</tr>
<tr>
<td><strong>CVR (mm Hg/ml/100 gm/min)</strong> (N = 4)</td>
<td>3.4 ± 0.4†</td>
<td>2.2 ± 0.4</td>
<td>1.9 ± 0.2</td>
<td>1.8 ± 0.2</td>
<td>1.7 ± 0.3</td>
<td>1.6 ± 0.2</td>
<td>2.0 ± 0.2</td>
</tr>
</tbody>
</table>

*All numbers mean ± SEM; N = number of different experiments in which measurements were made at hourly intervals.
†Statistically significant from two-hour value (P < 0.05; paired t-test).

### TABLE 2

**Response of CBF, MABP and CVR to SAH; ICP Normal (Group 2)**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After SAH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total CBF</strong> (N = 9)</td>
<td>51 ± 4.7</td>
<td>67 ± 8.2</td>
</tr>
<tr>
<td><strong>Occipital CBF</strong> (N = 5)</td>
<td>32 ± 3.1</td>
<td>53 ± 7.2</td>
</tr>
<tr>
<td><strong>Parietal CBF</strong> (N = 5)</td>
<td>33 ± 8.4</td>
<td>39 ± 13.0</td>
</tr>
<tr>
<td><strong>Reticular CBF</strong> (N = 9)</td>
<td>69 ± 13.0</td>
<td>100 ± 18.0</td>
</tr>
<tr>
<td><strong>Thalamic CBF</strong> (N = 9)</td>
<td>51 ± 11.0</td>
<td>77 ± 20.0</td>
</tr>
<tr>
<td><strong>Hypothalamic CBF</strong> (N = 7)</td>
<td>42 ± 8.7†</td>
<td>59 ± 11.0</td>
</tr>
<tr>
<td><strong>Frontal CBF</strong> (N = 5)</td>
<td>50 ± 7.7</td>
<td>86 ± 18.0</td>
</tr>
<tr>
<td><strong>MABP (mm Hg)</strong> (N = 9)</td>
<td>103 ± 8.0</td>
<td>100 ± 4.0</td>
</tr>
<tr>
<td><strong>ICP (mm Hg)</strong> (N = 9)</td>
<td>5 ± 1.0</td>
<td>6 ± 2.0</td>
</tr>
<tr>
<td><strong>CVR (mm Hg/ml/100 gm/min)</strong> (N = 9)</td>
<td>2.1 ± 0.2</td>
<td>1.5 ± 0.1</td>
</tr>
</tbody>
</table>

*All numbers mean ± SEM; N = number of different experiments in which measurements were made at hourly intervals.
†Statistically significant from two-hour value (P < 0.05; paired t-test).
Hashi et al.,21 who measured CBF in baboons for 60 minutes after a subarachnoid injection of blood and found CBF to increase and CVR to decrease during this time. Petruk et al.42 also studied the effect of SAH on CBF in the monkey. Although their methods were quite like ours in most important respects, their results were significantly different in that they noted a significant fall in CBF immediately after SAH, which persisted until the experiment ended three hours later. The difference between the results of Petruk et al.42 and ours may be explained by the manner in which blood was injected into the chiasmatic cistern to produce the SAH. Petruk et al.42 injected 4 ml of blood within 20 seconds. We found that this rapid a rate of injection would often increase the ICP to a level that would transiently surpass the mean arterial blood pressure. This unphysiological relationship leads to total temporary cessation of CBF that may itself be sufficiently injurious to the brain to cause swelling or edema and a subsequent fall in CBF.

Our results support the conclusion of Weir et al.,17 Hashi et al.,21 and others,8,26 that vasospasm is but one factor in the genesis of encephalopathy after SAH. Additional factors besides vasospasm are probably necessary and perhaps at times are more important in determining whether brain ischemia will complicate an SAH. Whether or not spasm leads to symptomatic ischemic encephalopathy seems to depend upon fac-

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**TABLE 3**

Response of CBF, MAP, and CVR to SAH: ICP increased (Group 3).

<table>
<thead>
<tr>
<th></th>
<th>Time in hours</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CBF</td>
<td>48 + 8.88</td>
<td>58 + 11.08</td>
<td>66 + 14.90</td>
<td>50 + 19.00</td>
<td>23 + 10.80</td>
<td>11 + 7.20</td>
</tr>
<tr>
<td>Occipital CBF</td>
<td>43 + 11.04</td>
<td>52 + 14.04</td>
<td>64 + 17.00</td>
<td>52 + 19.00</td>
<td>24 + 10.80</td>
<td>11 + 7.20</td>
</tr>
<tr>
<td>Petrosal CBF</td>
<td>46 + 11.04</td>
<td>54 + 14.04</td>
<td>64 + 17.00</td>
<td>52 + 19.00</td>
<td>24 + 10.80</td>
<td>11 + 7.20</td>
</tr>
<tr>
<td>Temporal CBF</td>
<td>48 + 11.04</td>
<td>56 + 14.04</td>
<td>66 + 17.00</td>
<td>52 + 19.00</td>
<td>24 + 10.80</td>
<td>11 + 7.20</td>
</tr>
<tr>
<td>Frontal CBF</td>
<td>37 + 11.04</td>
<td>51 + 14.04</td>
<td>63 + 17.00</td>
<td>51 + 19.00</td>
<td>23 + 10.80</td>
<td>11 + 7.20</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>121 + 6.00</td>
<td>125 + 6.00</td>
<td>115 + 6.00</td>
<td>119 + 6.00</td>
<td>120 + 6.00</td>
<td>120 + 6.00</td>
</tr>
<tr>
<td>CVR (mm Hg/100 gm/min)</td>
<td>6.0 + 1.0</td>
<td>6.2 + 1.0</td>
<td>6.3 + 1.0</td>
<td>6.4 + 1.0</td>
<td>6.5 + 1.0</td>
<td>6.6 + 1.0</td>
</tr>
</tbody>
</table>

*All numbers mean = SEM; N = number of different experiments in which measurements were made at hourly intervals.

---

**FIGURE 4**

Total CBF changes in Group 3 after hypertensive SAH, at arrow.

---

**TABLE 3**

Response of CBF, MAP, and CVR to SAH: ICP increased (Group 3).

<table>
<thead>
<tr>
<th></th>
<th>Time in hours</th>
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<th>7</th>
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<td>52 + 19.00</td>
<td>24 + 10.80</td>
<td>11 + 7.20</td>
</tr>
<tr>
<td>Petrosal CBF</td>
<td>46 + 11.04</td>
<td>54 + 14.04</td>
<td>64 + 17.00</td>
<td>52 + 19.00</td>
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<td>11 + 7.20</td>
</tr>
<tr>
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</tr>
<tr>
<td>Frontal CBF</td>
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<td>63 + 17.00</td>
<td>51 + 19.00</td>
<td>23 + 10.80</td>
<td>11 + 7.20</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>115 + 6.00</td>
<td>119 + 6.00</td>
<td>119 + 6.00</td>
<td>120 + 6.00</td>
<td>120 + 6.00</td>
<td>120 + 6.00</td>
</tr>
<tr>
<td>CVR (mm Hg/100 gm/min)</td>
<td>6.0 + 1.0</td>
<td>6.2 + 1.0</td>
<td>6.3 + 1.0</td>
<td>6.4 + 1.0</td>
<td>6.5 + 1.0</td>
<td>6.6 + 1.0</td>
</tr>
</tbody>
</table>

*All numbers mean = SEM; N = number of different experiments in which measurements were made at hourly intervals.

---

**FIGURE 4**

Total CBF changes in Group 3 after hypertensive SAH, at arrow.
EFFECT OF SIMULATED SAH ON CBF IN MONKEYS

FIGURE 3
Response of ICP and MABP to hypertensive SAH in a monkey of Group 3. Observe acute transient hypertension and bradyarrhythmias.

Factors known to affect tissue function in the field supplied by a partially occluded artery. These are the ischemia-modifying factors described by Fisher, Karp and Adams, which include collateral circulation, viscosity of blood, hypoxia, metabolic rate of the perfused tissue, and perhaps most important for the encephalopathy of SAH, cerebral perfusion pressure. Evidence has been presented by Hashi et al. and Petruk et al. indicating that SAH may impair the autoregulatory mechanisms that maintain a normal CBF in the presence of a changing perfusion pressure. Impaired autoregulation can account in part for the fall in CBF after SAH observed in three of seven monkeys of Group 3 (fig. 4) in which the ICP was allowed to rise. Moreover, it was in the monkeys of Group 3 that subarachnoid injections of blood were often followed by especially large temporary increases in mean arterial blood pressure and cardiac arrhythmias (fig. 5). After an increase to a mean of 200 mm Hg, the blood pressure of another animal in Group 3 subsequently fell to 70 mm Hg, the ICP increased to 45 mm Hg, and after three hours CBF fell to zero. The data from this one animal are largely responsible for the mean total CBF of Group 3 remaining below control values after the SAH (fig. 4). Observations such as these may provide a clue to an improved understanding of the encephalopathy that follows SAH.

SAH usually provokes an intense sympathetic discharge. Whether it is due to a direct effect of blood irritating the brain, or to the sudden increase of ICP, or both is not clear. In any case, one may postulate that the severe arterial hypertension caused by a sympathetic discharge overwhelms an already partially compromised autoregulatory mechanism. The attendant hyperperfusion leads to brain edema, which is believed to reduce CBF regionally by increasing brain tissue pressure. Seizures occurring after the SAH probably add to any edema already formed. The intense sympathetic discharge also has been implicated in the development of both cardiac arrhythmias and frank myocardial necrosis observed after SAH. Subsequently, CBF may fall if cardiac output and blood pressure decrease due to myocardial injury.

SAH also may reduce cerebral perfusion pressure by increasing ICP. In the clinical setting, SAH commonly increases ICP because blood cells interfere with drainage of CSF through the interstices of the subarachnoid space and the arachnoid villi. Any brain swelling would be expected to further increase ICP. Figure 6 summarizes diagrammatically the interplay of factors, aside from hematoma or hydrocephalus, which, we propose, determines whether or not ischemic encephalopathy develops after an SAH.

The hydrogen clearance method of measuring CBF is well suited to this type of study. It enabled us to measure simultaneously both total CBF, from the torcular electrode, and local tissue blood flow from three electrodes placed strategically in the diencephalon and three others in the hemispheres. Noteworthy was the absence of any preferential reduction in flow to the deep nuclear areas after an SAH — information that could not be obtained with most other techniques commonly employed to measure...
Hypothetical interplay of factors that lead to ischemic encephalopathy after SAH. Numbers in parentheses refer to references for the particular mechanism.

CBF. Changes of total CBF detected by the torcular electrode were followed closely by changes detected at the local level by the tissue electrodes.

CBF increased and CVR decreased during the first part of the experiment in both control monkeys (Group 1) and monkeys in Group 2. We suspect that the CBF and CVR changes were related to the single dose of pentobarbital (50 mg I.V.) given at the very beginning of the experiment. Presumably, as the pentobarbital was metabolized, CBF increased as its depressant effect on brain was dissipated. We have found the hydrogen clearance method of measuring CBF to be particularly sensitive in detecting reductions in CBF caused by even small doses (8 mg per kilogram I.V.) of pentobarbital, an effect commented upon by others.

Our method of injecting blood through a needle placed stereotactically into the chiasmatic cistern simulates more closely the naturally occurring event than do injections of blood into the cisterna magna, as some investigators have done. It is simple, relatively reliable and eliminates the need for surgery or radiographical control. Since the method only violated the subarachnoid space with needles, CSF usually did not leak from the subarachnoid space. This perhaps explains why we found that SAH without spinal drainage was followed by a significant and sustained increase in ICP, which could be returned readily to normal by spinal drainage. The failure of others to observe a persistently elevated ICP after experimental SAH may be related to an unrecognized CSF leak.

To summarize and conclude, we have cited our own experimental data as well as the literature to support the hypothesis that spasmogens in bloody CSF play only a limited role in the pathogenesis of ischemic encephalopathy that follows an SAH. Studies of acute spasm produced by topical application of blood or a
component of blood onto cerebral arteries, and its lysis by vasodilators, possess intrinsic scientific merit, but their relevance to the encephalopathy we encounter in patients after SAH appears uncertain. The search for an effective treatment of the encephalopathy of SAH continues. Our efforts will probably be more successful if we end our preoccupation with spasmolysis and, following the lead of the Houston group, \( ^{21, 98} \) consider instead therapies that mitigate the total insult inflicted upon the brain by SAH.

Acknowledgments

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flow in the monkey measured by hydrogen clearance. Stroke 5:512-517 (July-Aug) 1974


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