Effects of subarachnoid hemorrhage from puncture of the middle cerebral artery on blood flow and vasculature of the cerebral cortex in the cat

Takennori Yamaguchi, M.D., and Arthur G. Waltz, M.D.
Cerebrovascular Clinical Research Center, Department of Neurology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

Bilateral measurements of regional cortical blood flow (CBF) and the diameter of superficial cortical arteries were made before and after puncture of the right middle cerebral arteries (MCA) of 11 cats with bilateral craniectomies. The CBF was decreased in the right cerebral hemispheres before puncture, probably because of manipulation and exposure of the MCA. Decreases of CBF occurred after MCA puncture in the contralateral cerebral hemispheres of five of seven animals without subarachnoid blood over the convexities of the hemispheres. The mean CBF value for the contralateral hemispheres was significantly lower after puncture than before. There was no consistent relationship between CBF and the calibers of surface cortical arteries. Thus, basal subarachnoid bleeding can cause decreases of CBF of the cerebral hemispheres, probably because of basal arterial spasm associated, at times, with vasomotor paralysis and failure of autoregulatory responses. If combined with increases of intracranial pressure, such decreases of CBF may be adequate to produce cerebral ischemia.

Key Words: cerebral cortical blood flow, cerebral autoregulation, subarachnoid hemorrhage, middle cerebral artery, cerebral cortex, cat

After spontaneous intracranial subarachnoid hemorrhage, patients frequently develop focal neurological deficits, and the brains of patients or animals that die from subarachnoid hemorrhage may have widespread patchy ischemic infarcts. The causes of the neurological dysfunctions and the ischemic infarcts are not fully known; one possible factor is focal ischemia due to severe arterial or arteriolar constriction. Many studies using angiography or other techniques to demonstrate vessel size have shown that spasm or marked narrowing of intracranial arteries, particularly major cerebral arterial trunks, can occur in patients with ruptured intracranial aneurysms and in animals with experimental subarachnoid hemorrhage. In animals, however, it may be difficult to demonstrate arterial spasm by angiography, and on neurological examination there usually is no evidence of focal cerebral ischemia.

Because the present report is concerned with the possible effects of secondary intracranial vascular spasm, not its cause, and be-
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cause many recent reports have included re-
views, a detailed survey of the literature will
not be attempted. Others have reported stud-
ies of the cerebral vasculature in which the
topical or systemic application of drugs or
blood has been used to clarify the nature of
possible spasmodenic substances that may
cause arterial narrowing.\textsuperscript{12,13,16,20,23,26,28}
Several studies have shown that blood can
cause constriction of cerebral vessels, 
\textsuperscript{12,20,22,23}
but the relationship of spasm to the
pathogenesis of the ischemic cerebral in-
farcts associated with spontaneous sub-
arachnoid hemorrhage is still not clear.

A decrease of the caliber of an artery has
little effect on the flow of blood through the
artery until the lumen reaches a critical size,
\textsuperscript{6,10,11,24,25,36}
yet studies of the cerebral cir-
culation in patients with ruptured intracra-
nial aneurysms often have shown decreases
of blood flow\textsuperscript{17,19,48} or prolongation of circu-
lation time.\textsuperscript{7,92} A decrease of cerebral blood
flow could be due to spasm of cerebral arte-
ries or to compression of the cerebral vascu-
lature by increased intracranial pressure or
increased tissue pressure from cerebral
edema. In the present investigation, the re-
sponses of cortical blood flow and of the cor-
tical vasculature of the convexities of the
cerebral hemispheres were studied in ani-
mals with bilateral craniectomies after punc-
ture of a middle cerebral artery at its origin.
Increases of intracranial pressure could not
occur because of the craniectomies, so that
the direct influence of hemorrhage at the
base of the brain, where ruptured intracra-
nial aneurysms are most frequently found,
could be determined.

Methods

Eleven adult cats were used for this study.
Each animal was anesthetized with halo-
thane and maintained in light anesthesia
through a tracheal stoma. The animal then
was placed in a headholder. With an opera-
tion microscope, the right middle cerebral
artery (MCA) was approached extraduraily
and exposed in the surgical field by dissec-
tion of the arachnoidal membrane.\textsuperscript{17,19,48}
The right temporal lobe was retracted gently
from outside the dura with a contoured self-
retaining retractor to avoid additional ma-
nipulation of the brain at the time of MCA
puncture.

Catheters filled with heparinized saline
were placed: 1) in the aorta through the
femoral artery for monitoring systemic arte-
rial blood pressure (MABP) and cardiac
rate, 2) in the vena cava through the femo-
ral vein for injection of drugs, and 3) in the
brachiocephalic artery through the right sub-
clavian artery for injection of a diffusable ra-
dioactive indicator for measurement of corti-
cal blood flow (CBF).

Bilateral craniectomies were made over
the convexities of the cerebral hemispheres,
and the surfaces of the brain were covered
with thin sheets of Saran for protection. Electroctricograms were recorded from
both hemispheres by screw electrodes placed
on the intact dura through the skull near the
cranietomies. Rectal temperature was moni-
tored continuously with a thermometer and
was kept near 37°C with a heating pad con-
trolled thermostatically.

After completion of the surgical proce-
dures, a minimal dose of d-tubocurarine was
injected intravenously, and the animals were
ventilated mechanically to maintain arterial
pCO\textsubscript{2} relatively constant.

The CBF was measured from the ectorso-
vian gyri of the convexities of both cerebral
hemispheres simultaneously, by external de-
tection of the beta activity of krypton-85 in-
jected into the brachiocephalic artery. The
CBF was calculated by kinetic analysis of
the data.\textsuperscript{3,38}

Observations and macrophotographs of
the superficial cortical vasculature were
made from the same gyrus as the measure-
ments of CBF, or the adjacent Sylvian gyrus,
at the time of each measurement.\textsuperscript{48} Addi-
tional photographs were taken after MCA
puncture, at 30 sec, 1, 2, 5, 8, and 10 min,
and every 10 min thereafter.

Changes of caliber of cortical arterial ves-
sels of 50 to 300 microns (\mu) in diameter
were determined from the photographic
prints. Changes of caliber of more than 10% 
were arbitrarily considered to be meaningful.

After two or three sets of measurements
of CBF and macrophotographs of the sur-
face vessels had been made, the right MCA
was punctured with the tip of a No. 11 knife
blade to produce a subarachnoid hemor-
rhage. Bleeding from the punctured MCA
usually stopped within several minutes. After
puncture, the first measurement of CBF was
Subarachnoid Hemorrhage

Bilateral basal subarachnoid hemorrhage occurred in each of the 11 animals after MCA puncture (Fig. 1). The basal hemorrhage was more marked on the right side in five animals, was symmetrical in six animals, and was more marked on the left side in one animal. In five animals the subarachnoid blood spread to the convexities of the hemispheres, including the regions from which measurements of CBF and arterial caliber were made. The hemorrhage over the convexity was symmetrical in three, there was more blood on the left side than on the right in one, and the blood spread only over the right hemisphere in one. After active bleeding from the MCA had stopped, the amount and distribution of subarachnoid blood did not change.

Effects on Cortical Blood Flow

From 72 pairs of bilateral measurements of CBF made in the 11 animals, three pairs from each animal were used for analysis: the measurements made just before MCA puncture, those made just after puncture (begun within 2 to 9 min), and those made late after puncture (begun after 28 to 109 min) (Table 1). Because blood on the surface of the brain may trap $^{85}$Kr in solution and interfere with accurate measurement of CBF, separate analyses were done for data obtained from animals without subarachnoid hemorrhage over the convexities of the hemispheres. Technical difficulties prevented accurate measurement of CBF early after puncture in Cat 4. In Cats 9 and 11, blood over the cortex prevented measurements of CBF and arterial caliber late after puncture.

The CBF of the hemispheres opposite the punctured MCA decreased early after puncture in six of 10 animals (Table 1). The decrease persisted in five of the six animals, but in Cat 3, the CBF returned to the pre-puncture value 39 min after puncture. The CBF decreased only late after puncture in two animals. In three of the 11 animals, no decrease of CBF was detected. When the data from the seven animals without blood over the convexities of the hemispheres were analyzed, the CBF was found to have decreased at some time in five: both early and late after puncture in two, only early in one, and only late in two. The means of the CBF values from all animals and from the seven without blood over the convexities were lower both early and late after puncture than before puncture (Table 1); the differences were statistically significant.

In seven of the 11 animals, CBF values from the hemisphere on the same side as the punctured MCA were lower than those from the opposite hemisphere even before puncture (Table 1). The mean of the CBF values from all hemispheres on the side of the punctured MCA likewise was lower than the mean of values from the opposite hemispheres, and the difference was statistically significant (Table 1).

The CBF of the ipsilateral hemisphere was found to be decreased early after MCA puncture in six of 10 animals, but five of these had subarachnoid blood over the cerebral convexity (Table 1). The means of the CBF values obtained before and early after puncture from the six animals without blood over the cortex were not significantly differ-

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Fig. 1. Cat 8. Base of the brain, showing the extent and severity of the bilateral basal subarachnoid hemorrhage after puncture of the right MCA. Hemorrhage was more severe on the right side.

begun within 10 min, and CBF was measured repeatedly (up to six times) for 2 hrs. The brain then was removed and inspected.

Results

Subarachnoid Hemorrhage

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The CBF of the ipsilateral hemisphere was found to be decreased early after MCA puncture in six of 10 animals, but five of these had subarachnoid blood over the cerebral convexity (Table 1). The means of the CBF values obtained before and early after puncture from the six animals without blood over the cortex were not significantly differ-
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TABLE 1
Effect of puncture of the right middle cerebral artery on cortical blood flow

<table>
<thead>
<tr>
<th>Cat No.</th>
<th>Time after Puncture (min)</th>
<th>MABP* (mm Hg)</th>
<th>PaCO2 (torr)</th>
<th>Left Hemisphere</th>
<th>Right Hemisphere</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>before</td>
<td>92</td>
<td>34</td>
<td>1.53</td>
<td>1.33</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>111</td>
<td>36</td>
<td>1.52</td>
<td>1.41</td>
</tr>
<tr>
<td></td>
<td>46</td>
<td>90</td>
<td>36</td>
<td>1.49</td>
<td>1.28</td>
</tr>
<tr>
<td>3</td>
<td>before</td>
<td>92</td>
<td>30</td>
<td>2.02</td>
<td>1.44</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>105</td>
<td>32</td>
<td>1.99</td>
<td>1.46</td>
</tr>
<tr>
<td>5</td>
<td>before</td>
<td>96</td>
<td>34</td>
<td>1.35†</td>
<td>1.10†</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>126</td>
<td>34</td>
<td>1.63</td>
<td>1.16</td>
</tr>
<tr>
<td>7</td>
<td>39</td>
<td>126</td>
<td>32</td>
<td>1.55</td>
<td>1.41</td>
</tr>
<tr>
<td>8</td>
<td>before</td>
<td>93</td>
<td>34</td>
<td>1.43</td>
<td>1.74</td>
</tr>
<tr>
<td>9</td>
<td>86</td>
<td>93</td>
<td>38</td>
<td>1.42</td>
<td>1.63</td>
</tr>
<tr>
<td>10</td>
<td>before</td>
<td>120</td>
<td>38</td>
<td>1.60</td>
<td>1.44</td>
</tr>
<tr>
<td>11</td>
<td>109</td>
<td>148</td>
<td>33</td>
<td>1.38</td>
<td>1.36</td>
</tr>
<tr>
<td>12</td>
<td>60</td>
<td>137</td>
<td>36</td>
<td>1.10†</td>
<td>1.18†</td>
</tr>
<tr>
<td>13</td>
<td>before</td>
<td>105</td>
<td>43</td>
<td>1.70</td>
<td>1.20</td>
</tr>
<tr>
<td>14</td>
<td>5</td>
<td>107</td>
<td>46</td>
<td>1.60</td>
<td>0.97‡</td>
</tr>
<tr>
<td>15</td>
<td>28</td>
<td>108</td>
<td>43</td>
<td>1.17‡</td>
<td>0.89‡</td>
</tr>
<tr>
<td>16</td>
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<td>34</td>
<td>1.35</td>
<td>1.07</td>
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<tr>
<td>17</td>
<td>6</td>
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<td>33</td>
<td>0.77‡</td>
<td>0.71‡</td>
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<tr>
<td>18</td>
<td>48</td>
<td>93</td>
<td>36</td>
<td>0.71‡</td>
<td>0.88‡</td>
</tr>
<tr>
<td>19</td>
<td>before</td>
<td>102</td>
<td>36</td>
<td>1.40</td>
<td>1.05</td>
</tr>
<tr>
<td>20</td>
<td>9</td>
<td>94</td>
<td>37</td>
<td>1.33</td>
<td>0.64‡</td>
</tr>
<tr>
<td>21</td>
<td>before</td>
<td>121</td>
<td>40</td>
<td>1.31</td>
<td>1.18</td>
</tr>
<tr>
<td>22</td>
<td>10</td>
<td>101</td>
<td>35</td>
<td>0.80‡</td>
<td>0.69‡</td>
</tr>
<tr>
<td>23</td>
<td>41</td>
<td>98</td>
<td>40</td>
<td>1.04‡</td>
<td>1.04</td>
</tr>
<tr>
<td>24</td>
<td>before</td>
<td>116</td>
<td>40</td>
<td>1.20</td>
<td>0.91</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>105</td>
<td>42</td>
<td>0.54‡</td>
<td>0.28‡</td>
</tr>
</tbody>
</table>

MABP = systemic arterial blood pressure; SAH = subarachnoid hemorrhage over convexity of hemisphere (absent = 0, present = +); CBF = cortical blood flow.

† Decrease of CBF probably due to puncture of middle cerebral artery.
‡ Decrease of CBF uncertain because of blood on cortex.
§ P<0.05 when compared to the mean of values obtained before puncture.
** P<0.05 when compared to mean of values obtained from left hemisphere.

ent (Table 1). The CBF of the ipsilateral hemisphere decreased late after MCA puncture in five of nine animals, two of which had subarachnoid blood over the convexity. The means of the CBF values obtained before and late after puncture from animals without blood over the cortex were not significantly different (Table 1).

Effects on Arterial Caliber

The changes of arterial caliber after MCA puncture were inconsistent (Table 2; Fig. 2). Constriction, dilatation, or both were noted, without obvious relationship to changes of CBF.

Miscellaneous Results

Constriction (spasm) of the right MCA
### TABLE 2

**Effect of puncture of the right middle cerebral artery on arterial caliber**

<table>
<thead>
<tr>
<th>Cat No.</th>
<th>Time after Puncture</th>
<th>Change of Arterial Caliber*</th>
<th>Left Hemisphere Vessel Diameter</th>
<th>Right Hemisphere Vessel Diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>50–100μ</td>
<td>100–200μ</td>
</tr>
<tr>
<td>1</td>
<td>early</td>
<td>0</td>
<td>M*</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>late</td>
<td>0</td>
<td>D</td>
<td>D</td>
</tr>
<tr>
<td>2</td>
<td>early</td>
<td>0</td>
<td>D</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>late</td>
<td>0</td>
<td>M</td>
<td>D</td>
</tr>
<tr>
<td>3</td>
<td>early</td>
<td>C</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>late</td>
<td>C</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>early</td>
<td>C</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>late</td>
<td>C</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>early</td>
<td>0</td>
<td>C</td>
<td>C</td>
</tr>
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<td>C</td>
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<tr>
<td>6</td>
<td>early</td>
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<td>0</td>
<td>0</td>
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<tr>
<td></td>
<td>late</td>
<td>0</td>
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<td>0</td>
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<tr>
<td>7†</td>
<td>early</td>
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<td>0</td>
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<td>0</td>
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<td>9§</td>
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<td>0</td>
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<td></td>
<td>late</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>10§</td>
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<td>0</td>
</tr>
<tr>
<td></td>
<td>late</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* C = constriction; 0 = no change; D = dilatation; M = mixed constriction and dilatation.
† Change possibly related to change of systemic arterial blood pressure.
‡ Subarachnoid hemorrhage, convexity of right hemisphere.
§ Subarachnoid hemorrhage, convexities of both hemispheres.

was seen regularly during exposure of the artery for puncture, particularly during dissection of the arachnoid.

Decreases of CBF correlated roughly with the extent of subarachnoid hemorrhage, as judged by inspection of the base of the brain after removal.

In two animals, the MABP increased more than 10 mm Hg after MCA puncture; in these animals, decreases of CBF did not occur (Table 1). Four animals (Cats 8, 9, 10, and 11) had decreases of MABP after puncture; all of these had subarachnoid blood over the convexities of the hemispheres.

Cardiac rate changed after MCA puncture only in Cat 9 (a decrease) and Cats 2 and 8 (an increase, late after puncture).

### Discussion

The methods used for this study of the cerebral vasculature have definite limitations, related particularly to the craniectomies, the manipulation of the MCA before puncture, the sizes of the observed arterial vessels, and the inability to observe the MCA and other basal vessels after puncture. Thus, the most important finding was that blood flow of the cortex of the contralateral hemisphere can be decreased by MCA puncture, even if subarachnoid blood does not spread to the convexity of the hemisphere. Because the decrease of CBF was not associated with cortical arterial spasm or with changes of MABP, cardiac rate, or PaCO₂, it must have been caused by constriction (spasm) of the major arteries at the base of the brain.

Simple manipulation of the basal cerebral arteries can cause decreases of CBF,† the spasm induced by manipulation and exposure of the right MCA in this study probably caused the decreases of CBF in the right cerebral hemispheres that occurred before arterial puncture. The failure of subarachnoid hemorrhage to produce additional decreases of CBF probably was due to the prior manipulation. Because there was no additional manipulation of the left MCA at the time of...
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puncture, the decrease of CBF of the hemisphere opposite the punctured artery was due to the basal subarachnoid bleeding.

No increases of CBF (reactive hyperemia) were found in the present study; there was no secondary vasodilatation30 during the relatively short period after puncture in which measurements of CBF were made.

The inconsistent responses of surface cortical arteries to basal subarachnoid bleeding probably were related to local vascular factors. Arterial constriction after puncture may have been due to propagation of spasm from vessels at the base of the brain, by neurogenic or myogenic mechanisms. Arterial dilatation after puncture probably was an autoregulatory response38 to decreased intraluminal pressure in the arteries, produced by basal vascular constriction. In most animals with dilatation, the autoregulatory response was not adequate to prevent a decrease of CBF. The failure of arterial caliber to change in many animals indicates that vasomotor paralysis to changes of MABP38 can occur with subarachnoid bleeding, although slight dilatation might have occurred and not have been detected. Vasomotor paralysis to changes of arterial pCO2 has been described previously.39 Vasomotor paralysis and failure of autoregulation may contribute to decreases of CBF caused by constriction of basal arterial vessels.

The finding of decreased CBF of the contralateral hemisphere after MCA puncture may be of added significance in this group of animals because of the bilateral craniectomies. The decreases of CBF were not caused by increases of cerebrovascular resistance (CVR) produced by increases of intracranial pressure; the increases of CVR must have been related to the direct effect of basal subarachnoid blood on basal arterial vessels. The decreases of CBF were slight and probably not adequate to cause cerebral infarction. However, an associated increase of intracranial pressure may cause a superimposed increase of CVR in brain tissue such that focal or generalized cerebral ischemia could develop; a combination of basal arterial spasm and increased resistance distally may cause the neurologic dysfunctions and ischemic infarcts that occur after subarachnoid hemorrhage.

Acknowledgments

Technical, instrumentation, and analytic assistance were provided by Robert D. Oststrom, Robert E. Anderson, and the Mayo Clinic Computer Facility.

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Received for publication December 4, 1970. This investigation was supported in part by Research Grant NB-6663 from the National Institutes of Health, U.S. Public Health Service.

Address reprint requests to: Arthur G. Waltz, M.D., Mayo Clinic, Rochester, Minnesota 55901.