Restoration of Middle Cerebral Artery Flow in Experimental Infarction*

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At the present time a patient with an acute middle cerebral artery occlusion represents an unanswered challenge for effective treatment. Conservative management has done little to alter the size of the resulting cerebral infarctions and the magnitude of related neurological deficits. Although occasional young persons withstand this catastrophe, these patients generally do poorly, and the survivors can hardly be called therapeutic successes.

The purpose of this work was to determine what benefits and hazards might be anticipated if flow through an occluded middle cerebral artery could be restored. Possible protective measures of hemodilution were investigated, and particular attention directed to the problem of hemorrhagic cerebral infarction. Information of this nature is of utmost importance in determining the feasibility of middle cerebral artery surgery. The isolated but dramatic reported results serve to stimulate further studies and investigation so that such procedures can be undertaken more often and with reasonable hope of success.

This study is based on experimental procedures in 100 squirrel monkeys and 35 cats. The squirrel monkey was used in the studies of massive cerebral infarction, the cat in those of smaller lesions. The necessity for two models was determined by previous studies and concurrent clinical experience emphasizing the difference between the two sizes of infarction.

Materials and Methods

Massive Cerebral Infarction (Monkeys)

The monkey used was the squirrel monkey (Saimiri sciureus), average weight 75 kg.

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The animals were anesthetized with 0.25 ml of sodium pentobarbital (Nembutal 50 mg/ml) injected into the intrapleural space with a 3/8 in. No. 25 hypodermic needle. The animals were utilized as acute or chronic preparations.

Acute Preparations. Tracheostomies were performed with the electrosurgical unit. The monkey was then placed in a Waltz headholder. A unilateral scalp flap was reflected with the electrosurgical unit. The origin of the right middle cerebral artery was exposed by the retro-orbital extradural approach under the operating microscope. Details of this approach have been described previously.5,13 The dura over the hemispheres was then excised under microscopic guidance and the cortex overlaid with a transparent sheet of plastic (Saran Wrap). The camera assembly, described previously, was then focused on a localized area of cortex.16 Mean systemic blood pressures were measured throughout the experiment by a Tycos manometer attached to a bubble trap in turn attached to a siliconized polyethylene catheter inserted into the exposed femoral artery. The animals were maintained at normotensive or hypertensive levels depending upon the type of experiment. The mean blood pressure ranged between levels of 80 and 120 mm Hg in the normotensive groups and between 120 and 160 mm Hg in the group treated with vasopressors. In no animal preparations did blood loss exceed 5 cc.

A miniature Mayfield clip was next applied, under microscopic control, to the previously exposed middle cerebral artery. The middle cerebral artery was occluded for 3 hours during which time cortical changes were recorded photographically. At the end of 3 hours the spring clip was removed from the middle cerebral artery and the major circulation reestablished. Photographic records were continued for another hour.
Twenty such animals were operated on, studied, and photographed. These animals were separated into three groups. The control group of 10 animals had no treatment during the 3 hours of middle cerebral artery occlusion. A second group of five animals received a combination of low-molecular-weight dextran and salt-poor human serum albumin in a dosage equal to that administered to the chronic animals treated with hemodilution (see below). In the third group of five animals, the systemic blood pressure was artificially elevated by the intermittent intravenous administration of metaraminol (aramine) in an average dosage of .025 mg/kg every \( \frac{1}{2} \) to 1 hour. The frequency of administration was governed by the animal's particular response to vasopressor and measured mean blood pressure.

**Chronic Preparations.** The animals were intubated with a small polyethylene tube and placed in an atraumatic headholder. A linear scalp incision was made with the cutting current of the Bovie electrosurgical unit. A small frontotemporal craniectomy was extended down the sphenoid wing. The middle cerebral artery was then approached under the operating microscope through a small dural incision overlying the optic nerve, an approach referred to and referenced above. The middle cerebral artery was occluded with a miniaturized Mayfield clip. This period of occlusion varied from 3 hours to permanent, depending upon the group classification of the animal. If the clip was removed, the wound was closed after its removal. If the clip was permanently applied, the wound was closed immediately. Maximum blood loss varied between 3 and 5 cc and no animals became hypotensive.

Animals were divided into the following groups (Table 1):

1. Control group of 10 animals. Middle cerebral artery was permanently occluded.
2. Control group of 10 animals, with hemodilution treatment. Middle cerebral artery was permanently occluded. The animals received 6 cc (1.5 gm)/kg of 25% salt-poor serum albumin plus 12 cc/kg of 10% low-molecular-wright dextran, the two agents being mixed and administered over a 1-hour period with the treatment starting 1 hour after

### Table 1

**Chronic squirrel monkey cerebral infarctions**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Animals</th>
<th>No. of Animals</th>
<th>Clinical State</th>
<th>Autopsy Findings</th>
<th>No. of Animals</th>
<th>Clinical State</th>
<th>Av. Time to Die</th>
<th>Autopsy Findings</th>
<th>Mortality &amp; Morbidity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCA, permanently occluded, no dilution</td>
<td></td>
<td>17</td>
<td>severe hemiplegic</td>
<td>large infarct</td>
<td>9</td>
<td>stuporous hemiplegic</td>
<td>24-26 hrs</td>
<td>severe edema</td>
<td>90 mortality, 10 morbidity</td>
</tr>
<tr>
<td>MCA, permanently occluded, dilution with Alb. &amp; LMWD</td>
<td>10</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCA, temporarily occluded 6 hrs, no dilution</td>
<td>10</td>
<td>0</td>
<td>1 hemiplegic</td>
<td>no deficit</td>
<td>6</td>
<td></td>
<td>иона</td>
<td>18-24 hrs</td>
<td>severe edema</td>
</tr>
<tr>
<td>MCA, temporarily occluded 6 hrs, dilution with Alb. &amp; LMWD</td>
<td>10</td>
<td>4</td>
<td>3 no deficit</td>
<td>no infarct</td>
<td>4</td>
<td></td>
<td>иона</td>
<td>18-24 hrs</td>
<td>severe edema</td>
</tr>
<tr>
<td>MCA, temporarily occluded 3 hrs, no dilution</td>
<td>10</td>
<td>0</td>
<td>no deficit</td>
<td>no infarct</td>
<td>4</td>
<td></td>
<td>иона</td>
<td>18-24 hrs</td>
<td>severe edema</td>
</tr>
<tr>
<td>MCA, temporarily occluded 3 hrs, dilution with Alb. alone</td>
<td>10</td>
<td>7</td>
<td>no deficit</td>
<td>no infarct</td>
<td>3</td>
<td></td>
<td>coma</td>
<td>4 hrs</td>
<td>severe edema</td>
</tr>
<tr>
<td>MCA, temporarily occluded 3 hrs, dilution with Alb. &amp; LMWD</td>
<td>20</td>
<td>4</td>
<td>no deficit</td>
<td>no infarct</td>
<td>16</td>
<td></td>
<td>iqueta</td>
<td>10-18 hrs</td>
<td>severe edema</td>
</tr>
</tbody>
</table>

MCA = middle cerebral artery
Alb. = 25% salt-poor human serum albumin
LMWD = low molecular weight dextran—10%—(Rheomacrodex)—supplied by Pharmacia Co.