Artificial Embolization of the Middle Cerebral Artery in Primates

DESCRIPTION OF AN EXPERIMENTAL MODEL WITH EXTRACRANIAL TECHNIQUE

BY ALFONSO M. BREMER, M.D., OSAMU WATANABE, M.D., AND ROBERT S. BOURKE, M.D.*

Abstract:
Artificial embolization of the middle cerebral artery (MCA) was produced in the primate, with a technique similar to that described by Luessenhop and Spence (1960) for the treatment of an inoperable arteriovenous malformation in the territory of the MCA. Silicone spheres (1 to 1.5 mm in diameter) were introduced into the internal carotid artery (ICA) via the external carotid artery (ECA). Emboli (1 to 1.3 mm) passed into the anterior cerebral artery (ACA) in 12%, and into the MCA in 50%. Emboli (1.2 to 1.5 mm) stopped at the ICA bifurcation in 54%. In all primates (82.35%) in which the emboli occluded the ICA bifurcation or the MCA, immediate contralateral hemiplegia developed. The correlation of the anatomical characteristics of the intracranial vasculature of the ICA bifurcation, the diameter of the emboli, and the anatomical localization of the silicone spheres suggests that this experimental model can produce a selective acute "point" occlusion of the MCA in at least 75% of the cases without violating the cranium, in which the resultant changes in the distribution of water and electrolytes in the brain during the acute ischemic event in the territory of the MCA of the primate can be studied.

Additional Key Words
primate stroke model middle cerebral artery embolism

The artificial embolization of the middle cerebral artery (MCA) in humans was reported by Luessenhop and Spence1 as a treatment for an inoperable arteriovenous malformation in the territory of the sylvian artery. Experimental MCA embolism (0.8 mm steel balls) was performed in dogs by Penry and Netsky,2 Molinari3 described cylindric emboli made with silicone rubber compound for segmental embolization of the MCA in the dog, and a similar method has been used in the primate.4

This report describes MCA occlusion due to artificial emboli introduced extracranially into the cerebrovascular anatomy of the macaque. The fate of the emboli and the role of the arterial width at various sites were studied.

Methods
Adult primates (Macaca mulatta), 3 to 4 kg body weight, were anesthetized with phencyclidine (0.25 mg per body weight) administered intramuscularly. Half of the initial dose was administered every hour of the experiment to maintain an adequate level of anesthesia. The primates had decreased corneal and pupillary reflexes and a minimum of movement in all four limbs (enough to assess any change in the muscle tone and grasping strength).

Each animal was secured by a stereotaxic headholder. Two intravenous catheters (PE 240) were inserted; one for a slow drip (30 ml per hour) of lactated Ringer's solution, and the other for venous blood sampling. A third catheter was inserted into the femoral artery for continuous monitoring of the arterial blood pressure and sampling. The arterial blood pressure was monitored with an arterial Statham transducer (Gilson recorder).

After preliminary recordings of the cardiac and respiratory rates, arterial blood pressure, and analysis of blood gases, the stereotaxic headholder was rotated 25° to the right and 10° down. A linear incision following the anterior edge of the sternocleidomastoid muscle was adequate for the dissection of the common carotid artery (CCA), internal carotid artery (ICA), and external carotid artery (ECA). The ECA was permanently ligated at the first lateral arterial branch. Silicone spheres (1 to 1.5 mm in diameter, 1.5 to 2 mg in weight) impregnated with barium particles (Heyer-Schulte Co., Santa Barbara, California) were used as emboli. Each embolus was measured, weighed, and introduced through a minimal arteriotomy in the ECA, while vascular clamps temporarily occluded the ICA and CCA. The ECA was proximally advanced into the lumen of the CCA, and a temporary ligature was applied at the origin of the ECA. The ICA blood flow was resumed by releasing the vascular clamps and the embolus was carried into the intracranial ICA system. The ECA was permanently ligated. The skin was reaproximated with Mitchell clips. Recordings of vital parameters and analysis of blood gases were repeated. Spontaneous respiration was maintained throughout the entire experiment.

At the end of the experiment, the primates were killed by the guillotine method. The brain and the intradural ICA were removed. The brain was fixed in a 10% solution of for-
The emboli were identified and the specimens with emboli in the anterior carotid artery (ACA), MCA and ICA were selected. After adequate fixation of the specimens, the width of the arterial origin of the ACA, MCA, and posterior communicating artery (PCA), and the terminal segment of the ICA were measured by microscopy. The lateral arterial angles of the ICA bifurcation and the rising angle of the PCA from the ICA were measured in the respective projection planes, considering that the main extension of the ACA and MCA is in the anteroposterior plane and for the PCA in the lateral plane. Photographs of the specimens in the pertinent projections were magnified; slides were projected on a screen to simplify the measurement of the angles.

### Results
Under magnification, the silicone spheres impregnated with barium particles were not perfect spheres. Emboli between 1.2 and 1.3 mm weighed 1.5 to 1.7 mg; other diameters of silicone spheres were correlated with respective weights (table 1).

The width of the arterial segment of origin of the ACA ranged from 0.41 to 1.0 mm, of the MCA from 0.50 to 1.16 mm, and of the PCA from 0.33 to 0.58 mm. The terminal segment of the ICA at the bifurcation ranged from 0.74 to 1.24 mm. The width of the origin of the MCA was greater than the ACA from the same ICA bifurcation in 76% of the specimens; in 19% the MCA segment of origin was the same width as the terminal segment of the ICA; and in 24% was the same as the ACA segment of origin (table 1). The aperture of the lateral angles made by the MCA-ICA ranged from 101° to 164°, and for the ACA-ICA from 84° to 114°. The difference among these lateral angles of the same ICA bifurcation ranged from 17° to 74° in 75% of 12 specimens (table 3). The angle made by the PCA-ICA was always under 90°.

Thirty-four emboli (1 to 1.5 mm in diameter) were placed at random. Sixteen (47.06%) of these were found in the MCA measuring 1 to 1.3 mm, four (11.76%) in the ACA measuring 1 to 1.1 mm, and 12 (35.39%) in the ICA bifurcation which measured 1.2 to 1.5 mm (two emboli not accounted for) (tables 4 and 5). Emboli that were from 1 to 1.1 mm in size always passed beyond the first arterial segment of the ACA and MCA (fig. 1), and in four instances, emboli of 1.2 mm passed into the insular portion of the MCA. The emboli were stopped at the M1 segment of the MCA or in the ICA bifurcation and measured 1.2 to 1.3 mm, and of two emboli of 1.5 mm size, one stopped at the ICA bifurcation and the other before the ICA bifurcation (table 6, fig. 2).

In primates with emboli (1 to 1.1 mm) in the ACA, the difference between the lateral angles of the ICA bifurcation ranged from 1° to 8°, while in the instances in which the emboli passed in the MCA these differences were between 17° and 74° (table 3). In every animal in which the embolus was found at the ICA bifurcation and in the MCA, contralateral weakness was immediately noticed. The weakness was usually flaccid and ranged from moderate to severe except in one case that presented some spasticity. In cases in which the embolus was found at the bifurcation, the angle made by the PCA-ICA was always under 90°.
ARTIFICIAL EMBOLIZATION OF THE MCA IN PRIMATES

TABLE 3
Anatomical Location of 34 Emboli (1 to 1.5 mm)

<table>
<thead>
<tr>
<th>Location</th>
<th>No. emboli</th>
<th>Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACA</td>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>MCA</td>
<td>5</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>ICA bifurcation</td>
<td>7</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>ICA</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Data obtained as a result of the acute "point" occlusion of the MCA and its effects on the distribution of water and electrolytes in the brain of the primate will be the subject of a subsequent report.

Discussion
The macaque was selected for our experiments because of the similarity of the cerebrovascular system to that of the human. The collateral arterial anastomoses from the extracranial arteries is less abundant than in the dog,7 the anastomosis between the right and left anterior cerebral arteries originates in a constant single pericallosal artery6,8 and an embolus occluding the origin of the ACA at the ICA bifurcation does not significantly decrease flow in the single pericallosal artery (due to the patency of the ACA anastomoses) (fig. 3).

The final route that an embolic particle follows at arterial bifurcations depends on the diameter of the embolus, the angle of branching, and the caliber of the artery at the bifurcation.

The silicone spheres impregnated with barium particles are available in different sizes. The relative inelasticity of the material limits the amount of molding which takes place, and there is little fragmentation of the emboli; few uncontrolled multifocal arterial occlusions are produced. The fate of the embolus within the ICA system appears to be dependent upon the diameter of the embolus selected. Therefore, the caliber of the artery and the angle of branching at the ICA bifurcation are important in determining the final position of the embolus.

![FIGURE 1](image1)

Two artificial emboli (1.1 mm) in the insular portion of the left MCA.

![FIGURE 2](image2)

Close-up view of the ICA bifurcation with two artificial emboli, 1.3 mm in size, occluding the origin of the left MCA (upper and right side of figure) and left ACA (left side of figure).
An embolus of 1.2 mm size in the ICA bifurcation occluding the origin of the left MCA and left ACA, which anastomoses with the right ACA and originates from a single pericallosal artery and remains without blood flow embarrassment. (Anteroposterior view of the ICA bifurcation showing the left MCA on the right side of figure.)

Despite the generally accepted belief that formalin-fixed arterial segments do not reflect the exact in vivo size of arteries, the measurements are of interest. Emboli, 1 to 1.1 mm in size, always passed beyond the ICA bifurcation and in 80% lodged in the MCA. In 76% of specimens the width of the origin of the MCA was greater than the ACA and the degree of aperture of the lateral angle made by the MCA-ICA was significantly greater (75%) than the ACA-ICA, thus facilitating the passage of the emboli beyond the M1 segment of the sylvian artery. Emboli larger than 1.1 mm did not pass into the ACA, although in four instances such emboli passed distally into the insular portion of the MCA. When emboli passed into the insular portion of the MCA, no emboli were found in a leptomeningeal artery.

Thus, by using emboli 1.2 to 1.3 mm in size, it is possible to occlude the M1 segment of the MCA or the ICA bifurcation in about 75% of instances (macaques). The immediate appearance of contralateral weakness indicated in every instance that an embolus had lodged at the ICA bifurcation or in the MCA. If similar experiments are to be extended for a longer period of time, sterile surgical technique and prophylaxis with antibiotics should be used.

Acknowledgment
We are very grateful for the professional advice of David C. McCullough, M.D., and the technical assistance in photography from Donald P. Shedd, M.D., and Isamu Hayata, Ph.D.

References
Artificial Embolization of the Middle Cerebral Artery in Primates: Description of an Experimental model with Extracranial Technique
ALFONSO M. BREMER, OSAMU WATANABE and ROBERT S. BOURKE

*Stroke*. 1975;6:387-390
doi: 10.1161/01.STR.6.4.387
*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1975 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/6/4/387

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org/subscriptions/