Experimental Cerebral Infarction. II. Clinicopathological Model of Deep Cerebral Infarction

BY GAETANO F. MOLINARI, M.D.

Abstract:
Experimental Cerebral Infarction. II. Clinicopathological Model of Deep Cerebral Infarction

Injection of silicone rubber cylinders into the internal carotid system permits selective occlusion of the proximal middle cerebral artery segment in the dog. Occlusions of this segment obstruct the mouths of the lenticulostriate arteries and result in deep cerebral hemisphere infarctions.

Surface vessels distal to the occluded segment remain patent and the cortex of the hemisphere is spared, due to efficient collateral circulation. Hemorrhage in cortical infarctions may occur distal to the point of vascular occlusion and, therefore, may be a function of patent meningo-cerebral anastomoses.

Hemorrhage into a deep infarction, however, occurred only when there was clinical and pathological evidence of distal migration of the embolus after an initial proximal occlusion. Infarctions of deep hemisphere structures were otherwise bland or "ischemic," probably because of the paucity of anastomoses among the penetrating blood vessels of the brain.

ADDITIONAL KEY WORDS
proximal middle cerebral artery
silicone rubber emboli
pathology
collateral circulation

Introduction

In a recent review of the anatomy of the blood supply of the forebrain in primates, Gillilan has reemphasized the role of the lenticulostriate arteries in clinical cerebral vascular disease.

While many methods have been devised to study cerebral infarction in laboratory animals, most techniques have dealt with phenomena occurring in the cerebral cortex caused by occlusion of pial arteries on the brain surface. Deep lesions of the internal capsule and basal ganglia have been described incidently in models producing infarction of an entire hemisphere, usually caused by large amounts of various types of embolic material.

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Injection of silicone rubber cylinders of selected length and diameter into the internal carotid system of the dog permits segmental occlusion of intracranial vessels. Occlusion of the proximal segment of the middle cerebral artery by this method obstructs the origins of the major penetrating vessels of the hemisphere, the lenticulostriate arteries.

This study describes the clinical and gross pathological features of cerebral infarctions caused by the selective occlusion of proximal cerebral artery segments, in contrast to lesions produced by occlusion of more distal meningo-cerebral vessels.

Methods

Twenty-five healthy mongrel dogs weighing 9.8 to 27.2 kg were subjected to unilateral dissection of the common, internal, and external carotid arteries, under pentobarbital anesthesia (5.0 mg/kg body weight). The internal carotid was directly cannulated using a 16-gauge or 17-gauge polyethylene needle. Care was taken to avoid
ARTERIOGRAPHICAL CHANGES

Results

Arteriography was not necessary to prove intracranial vascular occlusion because the embolic cylinders per se were radio-opaque.

However, using the method of Davis and Rumbaugh, high-fidelity arteriograms were obtained showing only the cerebral blood supply in five of the experiments. Before embolism, the vascular patterns in lateral projection were dominated by the internal carotid artery, the components of the circle of Willis and the middle cerebral artery and its branches. After proximal middle cerebral artery occlusion, the dominant vascular shadow was the anterior cerebral artery and its branches on the brain surface running toward the parasagittal region. By comparison to the preembolic studies the anterior cerebral was dilated. Figure 1 illustrates the characteristic arteriographical changes.

Clinical Observations

No significant clinical observations could be made upon the anesthetized animals.

During recovery from anesthesia, 15 of the 17 animals in the chronic group exhibited transient running movements of all extremities. These movements were phasic and alternated side to side, resembling natural running despite the posture of lateral recumbency and altered consciousness. Limb movements were more forceful on the unaffected side, but were present bilaterally.

As consciousness progressively increased, animals became quiet unless disturbed. During this period, tonic eye deviation toward the side of the lesion was the rule. The presence or absence of nystagmus varied with the level of consciousness. When aroused by loud noise or by tactile stimulation, the animals became anxious with the return of the crude running movements. During periods of agitation, there were apparent efforts to gain standing posture. These attempts were characterized by head, neck and torso deviation toward the side of the lesion and thrashing movements which occasionally caused the animals to roll over, strike the walls of the cage, or become wedged into corners in awkward postures.

Within 24 hours after surgery, all violent, thrashing, and running movements subsided. On the first postoperative day, five of the animals had improved to full consciousness, were relatively docile when approached, and were able to stand in their cages with a minimal amount of clumsiness, weakness or stiffness of the affected extremities. In these animals nystagmus had disappeared and head,
eye and neck postures were neutral; there was
tendency when moving about in their cages to
turn toward the side of the affected hemi-
sphere. By the second postoperative day, these
animals appeared normal in locomotion.

Nine of the animals had persistent head
and neck deviation with a crude clumsiness and
weakness of the contralateral extremities. Some
of the animals in this group were able to
achieve standing posture by the first postopera-
tive day, but ambulation was grossly impaired
by the stiffness of their affected extremities and
poor balance. There was a tendency to fall
toward the side of the hemiparesis. The paws
of the affected extremities frequently became
entangled in the floor grids, further complicating
their postural adjustments and attempts at
movement. By the second postoperative day,
two animals in this group remained recumbent
in a coiled posture with head and neck and
trunk deviated toward the affected hemisphere,
contralateral extremities in rigid extension.
Both these animals were difficult to rouse and
died spontaneously by the end of the third
postoperative day.

By the third postoperative day the seven
remaining hemiplegic animals had adapted
fairly well to their neurological deficit. These
animals walked continuously in a circle toward
the side of the lesion. Nystagmus was no longer
present. The affected extremities were generally
clumsy and stiff, but falling at this stage of
recovery was generally due to entanglement of
the affected paws in the floor grid. Two of
these animals had hemianopsia as well, ignoring food or water placed in the affected
field.

Animals 15 and 17 failed to follow this
general pattern. They showed no running
movements during recovery from anesthesia
but were akinetic and mute even after return to
apparent consciousness. They remained apa-
thetic and indifferent to food and water, never
attempted to stand although versive posturing
was absent, and rapidly developed dehydration
and inanition prior to sacrifice on the third and
fourth postoperative days.

Animal 16, in this series, showed signs of
severe hemiplegia with the usual head, eye,
neck, and torso deviations throughout the first
postoperative day. However, by the morning of
the second postoperative day, there had been a
dramatic improvement in the physical findings;
the animal sprang from its cage, was able to
walk with minimal signs of clumsiness of the
affected extremities, and no longer showed
head, eye or trunk version.

**Gross Pathological Changes**

**VASCULAR OCCLUSIONS**

Intracranial vascular occlusion occurred in all
experiments in this series. Tables 1 and 2
indicate the locations of the intracranial emboli
recovered at postmortem examination. Emboli
were found in the middle cerebral artery
underlying the anterior perforated substance in
15 specimens. Emboli measuring 1 mm in
diameter at the time of injection produced
segmental intracranial occlusions, but were less
predictable in their final site of obstruction.

Two emboli of this type were found in the
anterior cerebral artery distribution, two in the
posterior communicating artery, and another in
a meningocerebral branch of the middle
cerebral overlying the parietal lobe.

Figure 2A shows the appearance of the
ventral surface of the brain containing a
proximal middle cerebral artery embolus.
Distal to the occlusion, surface vessels were
more prominent over the affected hemisphere
in all of the chronic specimens (fig. 2B); the
diameters of these vessels were somewhat
larger than those of the control hemisphere,
and the lumina, although patent, contained
blood blackened by the formalin perfusate.

Showers of small emboli occluded multi-
ple meningocerebral arteries largely in the
hemisphere on the side injected but with
occasional particles found in the contralateral
hemisphere and in the posterior circulation.

**FIGURE 1**

A. Lateral projection angiogram, showing the intracranial arteries of dog before embolism.
The large ophthalmic artery is seen on the right.
B. Arrow marks site of middle cerebral artery occlusion. Two large anterior cerebral
arteries are now seen following the contours of the corpus callosum with branches palisading
in the vertical plane.
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### TABLE 1

<table>
<thead>
<tr>
<th>Experimental number</th>
<th>Survival after embolism</th>
<th>Occluded segments</th>
<th>Areas of gross tissue necrosis</th>
<th>Other pathological features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>3 hours</td>
<td>3 fragments in MCA* branches just distal to Sylvian fissure</td>
<td>None</td>
<td>—</td>
</tr>
<tr>
<td>2.</td>
<td>3½ hours</td>
<td>Proximal MCA</td>
<td>None</td>
<td>—</td>
</tr>
<tr>
<td>3.</td>
<td>4 hours</td>
<td>Proximal MCA</td>
<td>None</td>
<td>Congestion in lenticulostriate aa. of affected hemisphere</td>
</tr>
<tr>
<td>4.</td>
<td>4 hours</td>
<td>Proximal MCA</td>
<td>None</td>
<td>Congestion in lenticulostriate aa. of affected hemisphere; pallor of caudate</td>
</tr>
<tr>
<td>5.</td>
<td>4 hours</td>
<td>Proximal MCA</td>
<td>None</td>
<td>Congestion &amp; dilatation of lenticulostriate aa. bilaterally &amp; surface branches of MCA</td>
</tr>
<tr>
<td>6.</td>
<td>5 hours</td>
<td>Proximal MCA</td>
<td>None</td>
<td>Dilatation &amp; congestion of surface vessels of embolized hemisphere; pallor of ipsilateral caudate and thalamus</td>
</tr>
<tr>
<td>7.</td>
<td>6 hours</td>
<td>Proximal MCA</td>
<td>None</td>
<td>Slight swelling of caudate capsule, and thalamus; occasional punctate hemorrhages in deep structures; superficial extravasation surrounding embolus</td>
</tr>
</tbody>
</table>

* MCA = Middle cerebral artery.
†This specimen is illustrated in figures 2 & 3.

**ACUTE CEREBRAL CHANGES**

Table 1 summarizes the gross pathological findings in the specimens from the acute experimental series. In this group, surface vessels were dilated and congested at the site of occlusion and distal to the embolus. In coronal sections, penetrating arteries were seen cut in cross, tangential, and longitudinal planes in both hemispheres, but generally appeared to be more numerous, of larger caliber, and congested with blood on the side of the embolus (fig. 3). The deep nuclei and internal capsule were usually pale and slightly swollen, containing occasional punctate hemorrhages. Necrosis of tissue could not be identified in the gross. There were no hemorrhages on the brain surface in seven instances but in the one lesion of six hours' duration extravasation of blood around the occlusion was clearly evident (fig. 2).

**CHRONIC CEREBRAL CHANGES**

Pathological changes were well developed in all specimens from animals surviving 24 hours or more. The correlation between segmental occlusion and the distribution of infarction in experiments 9 through 20 are summarized in table 2. Occlusion of the proximal middle cerebral artery segment underlying the anterior perforated substance consistently produced infarction of the caudate nucleus, the internal capsule, and the anterior thalamic nuclei. Infarctions of these deep structures were characteristically bland, showing varying degrees of dusky discoloration of the swollen deep gray matter masses (fig. 4).

Occasional small punctate hemorrhages were seen along the course of the lenticulostriate vessels toward the periphery of the zone of frank infarction.

In each case of proximal segmental occlusion, there was an irregularly shaped superficial infarction involving cortical structures immediately surrounding the embolus...
### TABLE 2

<table>
<thead>
<tr>
<th>Experiment number</th>
<th>Survival after embolism</th>
<th>Occluded segments</th>
<th>Areas of bland necrosis</th>
<th>Areas of hemorrhagic infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.</td>
<td>24 hours</td>
<td>Left proximal MCA</td>
<td>Head of caudate, internal capsule, anterior thalamus</td>
<td>Ventral cortex surrounding embolus; punctate extravasation in internal capsule</td>
</tr>
<tr>
<td>10.</td>
<td>36 hours</td>
<td>Left proximal MCA</td>
<td>Head and body of caudate, internal capsule, anterior thalamus</td>
<td>Cortex surrounding embolus; several punctate areas at periphery of deep lesion</td>
</tr>
<tr>
<td>11.</td>
<td>36 hours</td>
<td>Left post. communicating art.</td>
<td>Posterior internal capsule, body of caudate, lateral thalamus, hippocampus</td>
<td>Ventromedial temporal lobe cortex (surrounding embolus); hypothalamus patchy extravasations in hippocampus</td>
</tr>
<tr>
<td>12.</td>
<td>48 hours</td>
<td>Rt. post. communicating art.</td>
<td>Posterior internal capsule, lateral thalamus, body of caudate, hippocampus</td>
<td>Ventromedial temporal lobe cortex (adjacent to embolus)</td>
</tr>
<tr>
<td>13.</td>
<td>2 days</td>
<td>Left proximal MCA</td>
<td>Internal capsule, anterior thalamus, head and body of caudate</td>
<td>Ventral, frontal cortex &amp; temporal pole around embolus</td>
</tr>
<tr>
<td>14.</td>
<td>3 days</td>
<td>Left proximal MCA</td>
<td>Internal capsule, caudate pallidum</td>
<td>Cortex surrounding embolus, punctate lesion in pallidum near periphery of infarction</td>
</tr>
<tr>
<td>15.</td>
<td>3 days</td>
<td>Right anterior cerebral artery</td>
<td>Anterior corpus callosum</td>
<td>Patchy extravasation in right cingulate gyrus</td>
</tr>
<tr>
<td>16.</td>
<td>3 days</td>
<td>Meningocerebral branch of left MCA, over parietal lobe convexity</td>
<td>Anterior internal capsule, pallidum rostral caudate</td>
<td>Deep hemorrhage in capsule &amp; pallidum punctum in cortex at site of occlusion, large cortical area surrounding patent proximal MCA</td>
</tr>
<tr>
<td>17.</td>
<td>4 days</td>
<td>Anterior communicating artery</td>
<td>Anterior corpus callosum</td>
<td>Small foci in both cingulate gyri</td>
</tr>
<tr>
<td>18.</td>
<td>5 days</td>
<td>Left proximal MCA</td>
<td>Head of caudate</td>
<td>None</td>
</tr>
<tr>
<td>19.</td>
<td>10 days</td>
<td>Left proximal MCA</td>
<td>Caudate, capsule, thalamus</td>
<td>None</td>
</tr>
<tr>
<td>20.</td>
<td>18 days</td>
<td>Right proximal MCA</td>
<td>Caudate, pallidum, capsule thalamus</td>
<td>None</td>
</tr>
</tbody>
</table>
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FIGURE 2

A. Ventral surface of dog brain, fixed in situ, six hours after embolism. The occlusive bolus is surrounded by an area of superficial hemorrhage.

B. The convexities reveal the prominence of the meningeocerebral vessels of the infarcted hemisphere.

FIGURE 3

Serial coronal sections showing early changes of deep cerebral infarction six hours after proximal occlusion of the left middle cerebral artery. At the level of the optic chiasm, lenticulostriate vessels of both hemispheres are prominent in cross, oblique and longitudinal planes. At the level of the mammillary bodies the caudate nucleus is pale and there is swelling of the internal capsule on the affected side. Punctate hemorrhages are evident in the capsule, caudate, and amygdala.

(fig. 2A). These superficial lesions were easily recognized because they were grossly hemorrhagic, stained with formalin-fixed blood. Only in specimen 16 was there indication of deep extravasation of blood into the internal capsule or deep gray matter structures that approximated the intensity of hemorrhage seen in the

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Coronal sections of deep infarction 30 hours after embolism. The upper section demonstrates swelling, dusky discoloration and the glistening friable appearance of the caudate nucleus. The area of cortical infarction on the ventral surface marks the site of the occlusive embolus. The lower section shows a large, cavitated, necrotic lesion involving the tail of caudate, thalamus, capsule and putamen.

cortical infarctions. Specimen 18 in this series contained a left proximal middle cerebral artery embolism, but showed only discrete cystic infarction in the caudate nucleus.

Both posterior communicating artery occlusions produced deep infarctions involving the ipsilateral hippocampus, white matter of the posterior limb of the internal capsule, and the posterior and lateral thalamic nuclei.

Consistent throughout this series of experiments was a remarkable sparing of the gray matter of the cerebral hemispheres distal to the site of occlusion. The only areas of cortical infarction found were those hemorrhagic lesions surrounding the occlusive bolus itself. Only in one specimen with proximal segment occlusion (fig. 4) was there an area of clearly defined cortical infarction distal to the embolus. That lesion was found in the paraventricular fissure, appearing at 3 o'clock in the coronal sections shown in the figure.

Gross edema of the cerebral hemisphere on the side of infarction was evident in specimens harvested within two to three days after infarction. Edema was not found in specimen 18 containing only a small lesion of the caudate nucleus nor in the more chronic specimens, 19 and 20. In these late chronic specimens, of ten and 18 days' duration (fig. 5), deep irregularly shaped cystic lesions were clearly demarcated and there was no distortion

Coronal section containing deep cerebral infarction 18 days after embolism of the proximal middle cerebral artery. Swelling of the affected hemisphere is not evident. The deep cystic lesion communicates with the ventral surface at the site of embolic occlusion, lateral to the optic chiasm.
of architecture by brain swelling. Although there was cortical necrosis in the usual site around the occlusive emboli, formed blood elements had been replaced by brownish heme pigments in the superficial lesions.

**CORTICAL INFARCTIONS**

Pathological changes in the animals receiving 20 to 30 small fragments of embolic material were generally confined to the cerebral cortex and superficial white matter. Individual areas of infarction surrounded each embolic fragment. Areas of cortical necrosis were heavily pigmented with blood, while the underlying white matter showed bland necrotic changes (fig. 6). Of considerable interest were the patchy, irregular areas of hemorrhage at some distance downstream to the embolic fragments, not directly associated with occlusive particles. Several areas of hemorrhage distal to the site of embolic occlusion can be seen in the figure.

**Clinicopathological Correlations**

The two animals showing apathy and akinesia both had anterior cerebral occlusions. Infarctions in these specimens involved the corpus callosum and the gray matter of the cingulate gyri. Lesions produced in the two instances of posterior communicating artery occlusion involved the lateral thalamus, posterior internal capsule, and the hippocampus on the same side while the bulk of the caudate and the more anterior portions of the capsule were relatively spared. Both these animals recovered standing posture and gait by the third postoperative day; they walked continuously in circles toward the side of the lesion with persistent head and eye deviation. They had hemianopsia on the same side as the motor deficiency, ignoring food and stationary objects in their affected visual fields. Hemianopsia was most likely due to the posterolateral thalamic lesion.

Persistent severe motor defects were seen only in animals which had sustained deep infarctions. The five animals given showers of small emboli all had extensive, patchy cortical infarctions which were usually hemorrhagic but had minimal neurological residua even on the first postoperative day. The two animals that died spontaneously had massive deep lesions involving internal capsule, caudate and thalamus. Frank necrosis, well-established cystic degeneration, and gross edema of the infarcted hemisphere characterized the primary lesion, while bowing of the midline distorted the architecture on the contralateral side (fig. 4). Contralateral compression by the swollen affected hemisphere was the most likely cause of the spontaneous deaths.

There was slight difference in the distribution of deep infarctions which correlated with the completeness of the occlusion of the middle cerebral artery segment. Most emboli in this segment impacted at the point of arborization of the middle cerebral artery in the anterior Sylvian fissure. Embolic cylinders, which were
EXPERIMENTAL CEREBRAL INFARCTION II

Serial coronal sections showing hemorrhagic infarction in deep structures of the left frontal lobe. In the upper section, patent anterior and middle cerebral arteries are seen in cross section. The solitary embolus in this specimen was found in a surface branch of the middle cerebral artery, distal to the lenticulostriate origins.

5 mm long at the time of injection, generally did not fill the entire length of the proximal segment. The first 1.5 to 2 mm of vessel, distal to the circle but proximal to the embolus, remained patent and consequently the most medial penetrating arteries were not occluded. Infarctions produced by emboli in this situation involved anterior thalamus, internal capsule and the body of the caudate nucleus. Cylinders which occluded the entire length of the segment also blocked the most medial penetrating arteries. Infarctions produced by such occlusions also involved the more anterior structures deep in the frontal lobes, including the head of the caudate, the pallidum, and the anterior limb of internal capsule.

In one experiment (18) the embolus was long enough to fill the entire proximal segment, but the diameter of the vessel was generous and the cylinder did not completely occlude the lumen. There was a redundant fold at the distal end of the embolus which prevented migration into a vessel of smaller diameter. A small infarction was found which was bland, cystic and entirely confined to the body of the caudate nucleus. Neurological findings in this animal were subtle, consisting of mild stiffness of both contralateral extremities, but without versive posturing or circling ambulation.

Experiment 16 deserves special comment. During the early recovery stages from anesthesia, head, neck and eye deviation and hemiparesis suggested successful occlusion of the proximal segment of the middle cerebral artery. Persistence of these findings through the first postoperative day was thought consistent with a deep hemispheric infarct. However, by the morning of the second postoperative day, the animal had improved dramatically, showing only mild stiffness of the affected extremities, as seen in animals with superficial cortical infarctions. Postmortem examination revealed an area of superficial hemorrhage on the ventral surface of the brain surrounding the proximal middle cerebral arterial segment. However, that segment was found to be completely patent, and the embolic fragment was found in a distal branch of the middle cerebral artery overlying the convexity of the parietal lobe. Coronal section of the brain showed a frankly hemorrhagic deep lesion of the internal capsule, pallidum, and caudate head (fig. 7).

Discussion
Injection of cylindrical silicone rubber emboli by this method offers an experimental model of deep cerebral infarction in the dog. Occlusion of the proximal middle cerebral artery segment produces ischemia and infarction of local cortical areas supplied by the superficial branches of the occluded segment but, more significantly, produces necrosis in the distribution of penetrating vessels arising from that segment. The distribution of infarctions suggests that the most medial penetrating arteries of the lenticulostriate group supply anterior forebrain structures such as the...
anterior limb of internal capsule, head of the caudate, and pallidum, while the more lateral vessels of this group supply the genu of capsule, body of the caudate, and the anteromedial thalamic nuclei. Occlusion of the posterior communicating artery disrupts the deep circulation to the hippocampus, posterolateral thalamic nuclei, including the lateral geniculate body, and the posterior limb of internal capsule. Anterior cerebral artery occlusions produce local infarction of cingulate gyri and corpus callosum and a clinical picture of akinesia, apathy, and inanition.

In contrast to these findings which largely parallel the known clinicopathological corollaries of human neurology, multiple areas of cortical infarction produced minimal neurological signs. Although hemorrhage complicated the cortical lesions, it did not seem to adversely affect the neurological outcome. Only animals with involvement of deep structures showed evidence of severe motor or sensory handicap.

A zone of hemorrhagic infarction was usually found involving the cortex surrounding the embolus, regardless of whether the occlusion was in a proximal arterial segment or in a meningocerebral branch. Subcortical lesions were bland or "ischemic," whether in territory supplied by named penetrating vessels, such as the lenticulostriates, or in the distribution of penetrating branches of the meningocerebral network. Such hemorrhagic areas were not found in the acute lesions less than six hours old, and in the ten-day-old and 18-day-old lesions, frank blood in surface infarcts had been replaced by heme pigments. These observations suggest that hemorrhage into an infarct is a relatively slow process developing over a period of hours to days and resolving over the course of days to weeks. The explanation of the patterns and distribution of lesions in this series of embolic experiments might lie in the anatomy and pathophysiology of the cerebral anastomoses.

The role of the meningocerebral anastomoses in human cerebrovascular pathology has been clearly established by Vander Eecken and Adams and by Vander Eecken. The dog is known to have free anastomoses among meningocerebral branches of anterior, middle, and posterior cerebral arteries as well as a functional circle of Willis. Our experiments indicate that proximal segmental occlusion of major intracranial arteries affects mainly the circulation to deep structures perfused by penetrating vessels arising from the occluded segment. The integrity of cortex distal to the site of occlusion can be adequately explained by the functional efficiency of the anastomotic network distal to the circle.

The penetrating vessels of the brain, however, have few, if any, precapillary anastomoses. Most anatomists are in agreement on this point. Carpenter and his associates, however, were able to demonstrate deep anastomoses between branches of the anterior choroidal artery and posterior choroidal artery in 42 of 45 hemispheres in a study of human material. Gillilan confirmed this anastomotic system among the same vessels in lower primates.

Little is known about the fields of supply of the ganglionic branches of middle and anterior cerebral arteries in the dog. Specific information is wanting regarding possible precapillary anastomosis among the lenticulostriate and other penetrating arteries of dog brain. V. P. Kubushkina found no precapillary anastomoses among strial arteries in dogs by means of microinjection studies, but other Russian authors disagreed with her on this point.

Applying the hypothesis of Shellshear that the arteries of the brain are phylogenetically and ontogenetically stable, it seems safe to assume that anastomoses among penetrating arteries are extremely rare in the dog, as has been shown in man and lower primates. The paucity of such collaterals would adequately explain the devastation of deep ganglionic structures and the internal capsule caused by segmental occlusion of the proximal middle cerebral artery, while the patent meningocerebral anastomotic network could account for the preservation of cortex distal to the occluded segment.

The concentration of precapillary arterial anastomoses on the surface of brain might also explain the fact that cortical infarcts were hemorrhagic, while deep infarcts, occurring in vascular fields with few arterial anastomoses, were bland or "ischemic."

Pathological findings in our series of specimens, embolized with showers of small particles, are similar to those produced by other methods using particulate embolic mate-
EXPERIMENTAL CEREBRAL INFARCTION II

rials. Using the silicone rubber material, however, offers advantages over autologous clot and other foreign bodies in that the emboli are radio-opaque and can be easily identified in pathological specimens. Correlation of the site of vascular occlusion with the site of infarction has been a major deficiency in the autologous clot technique. In our series, cerebral lesions caused by multiple small particles include hemorrhagic necrosis of cortex immediately surrounding the embolus and bland necrosis of the superficial underlying white matter. These findings parallel those of Penry and Netsky\textsuperscript{17} in their study of occlusions of single leptomeningeal arteries.

The explanation of small cortical hemorrhages at some distance downstream to the meningoencephal artery occlusions remains unclear. Figure 6A shows several such hemorrhages. It is perhaps significant that these hemorrhages appear at the periphery of the middle cerebral artery distribution in “watershed” zones between middle cerebral and posterior cerebral territories. The source of bleeding might, therefore, be restituted blood flow, retrograde, through the distal segment of the occluded vessels by way of the maximally dilated meningoencephal anastomoses.

Primary proximal occlusion with subsequent distal migration of cerebral emboli has been suggested as an important mechanism in the pathogenesis of hemorrhagic infarction. In their discussion of the pathological data presented by Fisher and Adams\textsuperscript{18} in support of this theory, Kubik and Hiller\textsuperscript{18} argued that cerebral emboli generally occupy surface blood vessels, and resulting infarctions are hemorrhagic because of the greater numbers of anastomoses and capillaries in cortical gray matter. If hemorrhage into an infarction is merely a function of the anatomy of the vascular field in which the lesion occurs, then distal migration of an embolus and restitution of blood flow through damaged vessels need not occur.

Primary proximal occlusion and later distal migration has been demonstrated by Dalai and associates\textsuperscript{10} by serial angiography in patients. Rumbaugh et al.\textsuperscript{20} have reported similar angiographical evidence of late distal migration or recanalization in dogs, using autologous clot emboli. The pathological findings in one specimen in our series can be explained rationally only by invoking this mechanism. Local superficial hemorrhage surrounding the proximal middle cerebral artery segment was a characteristic feature of proximal occlusions. In experiment 16, hemorrhage in this region associated with a deep hemispheric infarction indicated that the proximal middle cerebral artery had been occluded. However, the vessel was completely patent at autopsy and the embolic cylinder was recovered in a distal branch of the middle cerebral artery overlying the parietal lobe cortex. The deep lesion in the penetrating artery distribution was grossly hemorrhagic, a feature unique to this specimen and consistent with restitution of blood flow through previously occluded deep vessels.

In the dog, therefore, cortical infarctions are usually hemorrhagic whether or not migration of the embolus has occurred. Hemorrhage into a deep infarct, however, only occurred when the embolus moved distal to the origins of the initially occluded penetrating arteries.

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Nomenclature used in identifying structures and topographical landmarks in dog brains is after Lim et al.\textsuperscript{21}


ADDITION

In the article by M. G. Ettinger which appeared in the May-June issue of STROKE on page 139, it should have been noted that the coagulation laboratory is supported by funds from NIH Grant NB 3364.
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