Autoregulation in Acute Focal Ischemia
An Experimental Study

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SUMMARY  The autoregulatory capacity of areas of the cerebral circulation subjected to ischemia by acute middle cerebral occlusion has been assessed in experimental primates. Autoregulation was tested to a rise in blood pressure induced by aramine, and to a fall in blood pressure induced by exsanguination. Whole hemisphere autoregulation was substantially disturbed due to both increased blood pressure and lowered blood pressure, but fractionation of this response indicated that autoregulation to increased blood pressure was preserved in the parasagittal and intermediate zones of the hemisphere, and totally lost in the region of the sylvian opercula where middle cerebral occlusion had produced the most dense ischemia. In relation to reduced perfusion pressure, autoregulation was again widely impaired and assessment of the degree of impairment by areas indicated no significant difference between the areas of the sylvian opercula and the remainder of the lateral aspect of the hemisphere studied. Where the degree of ischemia in each individual electrode was assessed, however, it appeared that the degree of autoregulatory loss to decreased perfusion pressure was dependent upon the intensity of ischemia, and autoregulation was partially preserved in electrodes whose immediate post-occlusion flow values were greater than 40% of basal flow, but absent in electrodes whose flow values were less than 20% of basal flow. Retransfusion following exsanguination in animals with acute middle cerebral occlusion indicated that there was a linear relationship between the degree of reperfusion achieved by retransfusion and the intensity of ischemia induced by exsanguination following middle cerebral occlusion. Thus there was some support for the no-reflow phenomenon in intensely ischemic areas.

Introduction
THE CAPACITY of the cerebral circulation to maintain constant blood flow in the face of changing perfusion pressure has been known since the studies of Fog,1, 2 and has been amply confirmed by current blood flow techniques since then.3-5 The lower level of autoregulation has been established in serial studies as a progressive fall in blood flow at systemic blood pressures below 60 mm Hg3-6 and, more recently, an upper limit of autoregulation has also been established in studies by Strandgaard et al.7 Impairment of autoregulation has been recognized as an almost invariable concomitant of relatively mild brain injury of a variety of types, often insufficient to impair any other manifestation of circulatory or neurological function. Reivich et al.8 showed in relation to trauma that autoregulatory disturbance could be graded from an almost complete loss to a mild disturbance, and it has become almost widely accepted that after ischemic cerebral episodes there is inevitable disturbance of autoregulation in the affected hemisphere.9-12 In its most severe form, impairment of autoregulation may reach a level of 10 to 15-minute intervals. During each flow estimation the arterial blood, recurrent flow estimations being performed by transorbital dissection, and CO2 reactivity checked by addition of CO2 to the inlet of the Palmer pump. In five animals autoregulation was tested to an increase of blood pressure by aramine infusion (at a rate of 40 μg per minute). The middle cerebral artery was then occluded with a Scoville clip. Autoregulation was then assessed to aramine in the five animals previously infused with aramine. All the animals were then progressively exsanguinated by withdrawal of arterial blood, recurrent flow estimations being performed at 10 to 15-minute intervals. During each flow estimation the systemic arterial pressure was held constant. We defined

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Our previous chronic experiments17 had indicated that a chronic stroke of more than three years' duration was still associated with variable degrees of autoregulatory loss in the ipsilateral hemisphere. The present study was designed in an attempt to elucidate the relationship between the degree of blood flow impairment induced by an experimental stroke, and the degree of loss of autoregulation.

Methods
Twelve adult baboons (Papio cynocephalus) of either sex in the weight range of 8 to 14 kg were used in the study. The techniques of anesthesia and preparation have been described previously18, 19 and are only briefly restated here. The animals were tranquilized with phencyclidine, anesthetized with alpha-chloralose after intubation, and ventilated artificially to maintain an arterial PCO2 in the range of 38 to 43 mm Hg; measurements of systemic arterial pressure and end-tidal CO2 were made continuously. Episodic measurements of arterial pH, PO2, and PCO2 were made. The lateral aspect of the right cerebral hemisphere was exposed and an array of small platinum electrodes placed from the opercular region to the parasagittal zone. Five or six electrodes were used in each study. Blood flow was determined by adding hydrogen gas in a concentration between 5% and 7% to the pure oxygen on which the animal was normally ventilated, and clearance monitored from the cortex as previously described.

The proximal middle cerebral artery was exposed by transorbital dissection, and CO2 reactivity checked by addition of CO2 to the inlet of the Palmer pump. In five animals autoregulation was tested to an increase of blood pressure by aramine infusion (at a rate of 40 μg per minute). The middle cerebral artery was then occluded with a Scoville clip. Autoregulation was then assessed to aramine in the five animals previously infused with aramine. All the animals were then progressively exsanguinated by withdrawal of arterial blood, recurrent flow estimations being performed at 10 to 15-minute intervals. During each flow estimation the systemic arterial pressure was held constant. We defined
100% flow as the absolute value immediately before either the amine infusion or the commencement of exsanguination. Final estimations of flow were made in six animals following full reinfusion of blood.

Data Analysis

The most familiar concept in relation to autoregulation is the curve which shows the maintenance of cerebral blood flow (CBF) at a constant level over a prolonged change in blood pressure either above or below the norm. This curve, with its inflection to decreasing CBF at approximately 60 mm Hg, or to increasing CBF at 130 to 140 mm Hg systemic blood pressure (SBP), is familiar to everyone. It is difficult, however, to compare such curves quantitatively from one experiment to another. We therefore analyzed the data in different ways, relating autoregulatory capacity in the first instance to location on the hemisphere. We have previously established a gradation of ischemia over the lateral aspect of the baboon hemisphere, which we have categorized in three areas: area A, the immediate opercular zone; area C, the parasagittal zone; and area B, an intermediate zone on the lateral aspect of the hemisphere (fig. 1). Differences in autoregulation in these areas were calculated for each animal by establishing a ratio between the percent change of flow and the change in arterial pressure in absolute terms. This ratio, \( \Delta \text{flow} / \Delta \text{arterial pressure} (\Delta F/\Delta P) \) would have, with perfect autoregulation, a value of zero, and the value would increase as autoregulation became impaired. Pressure steps of 10 to 15 mm Hg were used in the study. The mean value for \( \Delta F/\Delta P \) throughout the period of exsanguination was calculated for all electrodes in area A in each animal, and then compared with the mean of all electrodes in the same animal in areas B and C. The ratio between mean A over mean B and C would be unity if the autoregulatory characteristics of the two zones were the same, greater than unity if autoregulation in area A were worse than in B and C, and less than unity if the reverse were the case.

During the experiments we noted a tendency for patchy, low-flow areas of pallor to appear in area A and also in area B. Flow values for hydrogen electrodes, which in this group of animals as in the previous group showed a reasonable gradation over areas A, B and C immediately after middle cerebral occlusion (table 1), showed a much greater scatter as flow began to fall with superadded exsanguinatory stress. It seemed, therefore, that comparison of autoregulatory capacity by region might be less appropriate than comparison of autoregulatory capacity by the initial degree of ischemia. We therefore tested autoregulation by classifying the degree of ischemia in three ranges: (1) least degree of ischemia in which flow following clip was greater than 40% basal flow; (2) flow was between 20% and 40% basal flow; and (3) immediate post-clip flow was less than 20% basal flow. The majority of electrodes with the third degree of ischemia were in area A, and the majority of electrodes with the first degree of ischemia in area C. Autoregulatory capacity was tested by averaging the flow over all electrodes for each degree of ischemia and deriving a regression against pressure within the range of 25 to 171 mm Hg. Autoregulation was also tested by restricting the calculation to the range of 60 to 151 mm Hg where the normal autoregulatory curve was substantially flat, the slope from previous data being calculated as 0.006.

Results

Basal Flows and the Effect of Middle Cerebral Occlusion

The mean regional flows measured under basal conditions in the three areas (A, B and C) defined in figure 1, before and after occlusion of the middle cerebral artery, are shown in table 1 and compared there with the corresponding mean flows in animals similarly anesthetized in the previous series. Basal flows in the present group were appreciably higher, although only in area A were they significantly different from the previous group (73.9 ± 26.7 ml/100 gm per minute as compared with 48.2 ± 12 ml/100 gm per minute, p < 0.01). Slight differences in the species of the current batch used may explain these basal differences. The effects of middle cerebral occlusion are closely comparable in the two groups.

![Figure 1. The zones of reference on the lateral aspect of the baboon hemisphere (from Symon et al.*).](http://stroke.ahajournals.org/
Autoregulation to Aramine Before and After Middle Cerebral Occlusion

Full Hemisphere Autoregulation

In five animals hemispheric blood flows were averaged from all electrodes and autoregulation tested with aramine infusion before and after middle cerebral occlusion. The findings are given in table 2. Before middle cerebral occlusion, an average increase in blood pressure of 28% was accompanied by a small change (6%) in flow. After occlusion, a rather smaller blood pressure change (24%) was accompanied by a small change (6%) in flow. After occlusion, an average increase in blood pressure of 28% was accompanied by 26% change in blood flow, suggesting that over the whole hemisphere there was a substantial impairment of the capacity of the circulation to adapt to increased blood pressure. The ranges of blood pressure tested were between 77 and 175 mm Hg before occlusion, and 83 and 145 mm Hg following occlusion.

Regional Autoregulation to Aramine Infusion

In five animals autoregulation was compared as change in flow over change in pressure for the grouped electrodes in each area, and compared with the ratio between flow and pressure change with aramine infusion following middle cerebral occlusion (table 3). In areas B and C, although there was an increase in flow to aramine infusion in several areas B and C than in area A, and this may represent an abnormally narrow range of autoregulation.

### TABLE 2 Whole Hemisphere Autoregulation to Aramine Before and After Occlusion

<table>
<thead>
<tr>
<th>Exp. no.</th>
<th>Before occlusion</th>
<th>During aramine</th>
<th>% Change</th>
<th>Before occlusion</th>
<th>During aramine</th>
<th>% Change</th>
<th>Before occlusion</th>
<th>During aramine</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>77</td>
<td>98</td>
<td>27.3</td>
<td>77.3</td>
<td>73.5</td>
<td>Nil</td>
<td>83</td>
<td>56.7</td>
<td>Nil</td>
</tr>
<tr>
<td>8</td>
<td>90</td>
<td>110</td>
<td>22.2</td>
<td>75.6</td>
<td>73.5*</td>
<td>Nil</td>
<td>100</td>
<td>12.0</td>
<td>106.6</td>
</tr>
<tr>
<td>9</td>
<td>117</td>
<td>175</td>
<td>49.6</td>
<td>127</td>
<td>161.5</td>
<td>+19</td>
<td>117</td>
<td>15.3</td>
<td>100.0</td>
</tr>
<tr>
<td>11</td>
<td>125</td>
<td>150</td>
<td>20.0</td>
<td>56.7</td>
<td>96.1</td>
<td>+11</td>
<td>127</td>
<td>14.2</td>
<td>140.0</td>
</tr>
<tr>
<td>12</td>
<td>113</td>
<td>137</td>
<td>21.2</td>
<td>79.5</td>
<td>78.4</td>
<td>Nil</td>
<td>110</td>
<td>22.7</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Mean percentage changes

\[ \text{Mean } \pm \text{SD} 28 \pm 12 \quad 6 \pm 9 \quad 24 \pm 19 \quad 26 \pm 24 \]

*Indicates hemisphere flow value corrected for CO2 reactivity.

### TABLE 3 Regional Effects of Occlusion on Autoregulation to Aramine

<table>
<thead>
<tr>
<th>Exp. no.</th>
<th>Before occlusion</th>
<th>After occlusion</th>
<th>Mean ΔF%</th>
<th>Mean ΔF%</th>
<th>Mean ΔF%</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>1.123</td>
<td>0.969</td>
<td>-0.136</td>
<td>0.825</td>
<td>-1.405</td>
</tr>
<tr>
<td>8</td>
<td>0.737</td>
<td>3.472</td>
<td>1.045</td>
<td>1.65</td>
<td>1.15</td>
</tr>
<tr>
<td>9</td>
<td>0.36</td>
<td>2.63</td>
<td>0.55</td>
<td>1.80</td>
<td>0.26</td>
</tr>
<tr>
<td>10</td>
<td>1.30</td>
<td>3.69</td>
<td>1.82</td>
<td>0.56</td>
<td>1.71</td>
</tr>
<tr>
<td>11</td>
<td>0.33</td>
<td>3.01</td>
<td>0.42</td>
<td>1.01</td>
<td>0.77</td>
</tr>
<tr>
<td>Mean</td>
<td>0.77</td>
<td>2.75</td>
<td>0.74</td>
<td>1.17</td>
<td>0.50</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean ±SD</th>
<th>±0.44</th>
<th>±1.08</th>
<th>±0.74</th>
<th>±0.53</th>
</tr>
</thead>
</table>

p <0.025 NS NS

**NS = not significant.**

The value $\Delta F/\Delta P$ was calculated for each electrode, and a mean value taken for all electrodes in each region. There is a significant increase in the ratio $\Delta F/\Delta P$ in area A (p <0.025), but not in areas B or C.
(p < 0.04), and both were significantly different from the flows obtained under similar conditions in the previous group of animals (p < 0.001). Between 25 and 50 mm Hg the flows for the third degree of ischemia were also significantly less than those for the first degree of ischemia (p < 0.01). It appears that autoregulation to diminished perfusion pressure is partially preserved in electrodes whose immediate post-occlusion average flow values are greater than 40% of basal flow, and absent in electrodes whose flow values fall to less than 20% of basal flow.

A stricter comparison of autoregulatory capacity is achieved, however, by restricting the calculation of autoregulation to the range of 60 to 150 mm Hg where the normal autoregulatory curve is substantially flat, the slope from previous data being calculated at 0.006. Flow decreases at mean arterial pressures below about 60 mm Hg. In the present experiments, therefore, following the application of middle cerebral clip the slope of the regression line of flow and mean arterial pressure in the range 60 to 150 mm Hg was calculated for each of the three degrees of ischemia, with the results shown in Table 5. The coefficient of correlation between flow and pressure was in each instance significantly different from zero (p < 0.01 in the second and third degrees of ischemia, and < 0.001 in the first). The slopes were all significantly different (p < 0.001) from the previously established control value of 0.006. Further, though the slopes of the third and second degrees of ischemia were not significantly different from each other, there was a significant difference between the first and third degrees (p < 0.001) and between the first and second degrees of ischemia (p < 0.005).

We also related the degree of ischemia to the slope of the regression line of percentage flow on pressure (averaged for each animal over all relevant electrodes, and finally averaged over all available animals), as shown in Figure 4. While the standard errors are large, there was a significant difference between the slopes for the first and third degrees of ischemia (p < 0.05), and the data suggest that increasing ischemia is associated with an increasing steepness of the autoregulatory slope.

Effect of Reinfusion Following Exsanguination in Focal Ischemia

In six animals, after the middle cerebral artery had been occluded for about two hours and the animal exsanguinated to a low level of systemic blood pressure (mean 41.7 mm Hg, SD = 10.7), the mean arterial pressure was substantially restored (mean 100.3 mm Hg, SD = 21.7) following reinfusion. The flows recorded by 44 electrodes in these animals were analyzed.

While there was no correlation between the flow following reinfusion and the flow remaining immediately after middle cerebral occlusion, there was a strong correlation (r = 0.81, p < 0.001) between the flow following and the flow just prior to reinfusion, as shown in Figure 5. It is clear that the tissue subjected to maximum ischemia by exsanguination reperfused least well following restoration of blood. Six electrode sites showed post-retransfusion flows of less than 2% of the post-clip value, having been subjected to

**Table 4 Relationship of Flow to Mean Arterial Blood Pressure, for Each of the Three Degrees of Ischemia**

<table>
<thead>
<tr>
<th>Range of mean arterial blood pressure (mm Hg)</th>
<th>Flow (% of immediate post-clip flow): mean ± SD</th>
<th>Degree 1</th>
<th>Degree 2</th>
<th>Degree 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-49</td>
<td>41.6 ± 16.0*</td>
<td>33.2 ± 10.6</td>
<td>15.1 ± 18.9*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 8</td>
<td>6</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>50-74</td>
<td>67.3 ± 23.2†</td>
<td>69.5 ± 70.0</td>
<td>39.8 ± 37.8†</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 21</td>
<td>14</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>75-99</td>
<td>91.6 ± 19.4</td>
<td>88.5 ± 50.1</td>
<td>125.0 ± 90.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 16</td>
<td>10</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>100-124</td>
<td>101.4 ± 14.5</td>
<td>115.4 ± 51.3</td>
<td>84.3 ± 21.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 10</td>
<td>14</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>125-149</td>
<td>114.6 ± 15.7</td>
<td>135.7 ± 33.9</td>
<td>168.7 ± 84.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 15</td>
<td>14</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>150-175</td>
<td>105.6 ± 39.1</td>
<td>126.1 ± 34.6</td>
<td>246.5 ± 241.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 4</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Significant differences: *p < 0.01, †p < 0.04, N = number of electrodes. These data are shown graphically in Figure 3.

**Table 5 Correlation of Flow and Mean Arterial Pressure in the Range 60 to 180 mm Hg, for Each of the Three Degrees of Ischemia**

<table>
<thead>
<tr>
<th>Degree of ischemia</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope of regression line of flow on MAP (in range 60-180 mm Hg):</td>
<td>0.006</td>
<td>0.44</td>
<td>0.68</td>
</tr>
<tr>
<td>Correlation: r =</td>
<td>—</td>
<td>0.77</td>
<td>0.28</td>
</tr>
<tr>
<td>p =</td>
<td>—</td>
<td>0.001</td>
<td>0.01</td>
</tr>
<tr>
<td>N =</td>
<td>18</td>
<td>24</td>
<td>24</td>
</tr>
</tbody>
</table>

Significant differences between slopes: [p < 0.001]

The column headed "control" refers to a previous series of animals in which MCA occlusion was not performed (see text).
essentially total ischemia by exsanguination. A relative hyperemia, that is, a post-retransfusion flow greater than 100% of flow following the middle cerebral clip, occurred at seven electrodes.

Discussion

There is general agreement that soon after an ischemic cerebral episode, widespread disturbance of autoregulation in the affected hemisphere occurs. Our previous work has indicated that such disturbance persists for some years after experimental stroke, although restricted to the area of infarct and its neighboring zones, the rest of the hemispherical circulation showing apparent return to normal autoregulation. In the present study, we attempted to define the relationship between the degree of ischemia produced by our standard experimental stroke and the impairment of autoregulatory capacity in the affected hemisphere. It is apparent from our data that autoregulation is profoundly disturbed over the whole hemisphere following acute middle cerebral occlusion, in line with clinical findings, and that the extent of this impairment is very much wider than the area involved in autoregulatory impairment three years after such an occlusion. There is, however, clear evidence of some preservation of autoregulatory capacity in the parasagittal area closest to the collateral supply, in this instance from the anterior cerebral artery.

Although an acute middle cerebral occlusion appears to produce ischemia of a density generally greater than that necessary to impair autoregulation, the experiments here reported show evidence of a link between the degree of ischemia and the extent of loss of the autoregulatory capacity. Thus, although no region showed normal autoregulation and all differed significantly from control animals in this respect, only the immediate area of the sylvian fissure showed an approximately linear relationship between perfusion pressure and blood flow such as would be present in an apparently paralyzed circulation. As the degree of ischemia became less dense, so a tendency to preserve autoregulatory capacity to diminished perfusion pressure became more evident. We have already defined the distribution and density of ischemia following acute middle cerebral occlusion, but in terms of the gradation of ischemia following middle cerebral occlusion it was impossible to fractionate impairment of autoregulatory capacity in precisely those same terms. A better fit of data was obtained by dividing the hydrogen electrodes into groups according to the extent of ischemia in each electrode. From this it became apparent that some autoregulation was maintained where

Figure 3. The relationship of blood flow expressed as a percentage of immediate post-clip flow to mean arterial pressure during induced hypotension from hemorrhage. Electrode sites have been categorized by the degree of reduction in flow produced by middle cerebral occlusion in three degrees: (1) a degree in which flow following middle cerebral occlusion was greater than 40% of basal flow, (2) a second degree in which immediate post-clip flow was between 20% and 40% of basal flow, and (3) a third degree in which immediate post-clip flow fell to less than 20% of basal flow. The autoregulatory profile in the first and second degrees is shown in figure 3a, while that of electrodes with the third degree of ischemia is shown in figure 3b.
rCBF was greater than 40% of control flow, although the autoregulatory curve still showed a pronounced shift to the right. It seems likely, therefore, that even in the least affected areas of such a circulation, the autoregulatory plateau is unlikely to extend below systemic blood pressure of 100 mm Hg.

Within these terms, however, it is essential to consider not only the systemic blood pressure to which the area of acute focal ischemia has been subjected, but also the exact perfusion pressure which may be present within the infarct itself. It is known\textsuperscript{18, 22} that the pressure distal to middle cerebral occlusion in the monkey is reduced from some 80% of mean systemic blood pressure following occlusion. Thus, in ten animals, middle cerebral arterial pressure after acute middle cerebral occlusion was 17.8 mm Hg (±3.7) when the mean systemic arterial blood pressure was 108.3 mm Hg (±15.7). The relationship between middle cerebral arterial pressure and systemic arterial pressure in these studies and also in the study reported by Jansen and Kanzow\textsuperscript{23} makes it plain that with reducing systemic arterial pressure the middle cerebral arterial pressure falls slightly in relation to systemic arterial pressure, so that it is unlikely that the figure of 20% of systemic blood pressure in the middle cerebral field would be exceeded during the exsanguination studies of the present series. Studies of pressure in collateral vessels\textsuperscript{24} have indicated that the field pressure in the collateral circulation is unaffected by middle cerebral arterial occlusion, and although there have been no detailed studies to indicate the distribution of gradients of pressure, it seems from the study of Symon et al.\textsuperscript{24} that within at least the major branches of the middle cerebral, the field pressure measured throughout is similar. From the distribution of electrodes showing ischemia of the second and third degree (< 40% of basal flow), it is certain that the input pressure to these areas of cortex would be less than 20% of systemic arterial pressure, while a proportion of those electrodes showing less than 40% ischemia are certainly outside the low pressure zone. Considering these blood pressure levels in relation to the data shown in figure 1, it is therefore clear that the autoregulatory capacity of the circulation has been stressed in areas A and B to a very low level of blood pressure indeed, and that the complete loss of autoregulation to diminished perfusion pressure at low systemic blood pressure must occasion no surprise.

The interaction of the vasodilator stimulus of ischemia with the vasodilator stimulus of further reduction in systemic perfusion pressure might well be expected to abolish the autoregulatory capacity to such reduced perfusion pressure, particularly since the likely levels of intravascular pressure in the more densely ischemic zones would then be extremely low. It might, however, be suggested that vasoconstrictor stimuli should still evoke an autoregulatory response in such embarrassed areas of the circulation. Such has been suggested, for example, in circumstances of competition between vasoconstrictor and vasodilator stimuli in
pulsed increases in perfusion pressure during hypercapnia. 

The same investigators, however, also showed that following middle cerebral occlusion a sudden increase in pressure directly applied to the middle cerebral circulation through catheterization of a major branch of the middle cerebral artery evoked a great increase in electromagnetically monitored flow in Labbe's vein, leaving no doubt that a substantial portion of the middle cerebral circulation showed paralysis of autoregulatory mechanism to superadded pressure. This has also emerged from the present studies; although no significant difference in autoregulatory capacity to increased perfusion pressure could be detected by the electrodes in the areas of lesser ischemia, there was evidence that considering either the hemisphere as a whole or more specifically the area of maximal ischemia, significant impairment of autoregulation to increased perfusion pressure occurred.

The apparent preservation of autoregulatory capacity to increased perfusion pressure in ischemic zones must also be considered in the light of probable intravascular pressure changes distal to substantial vascular occlusion, since such major afferent vessel occlusion will act as a substantial buffer to hypertensive flow increases produced by elevation of the systemic blood pressure. They will, on the other hand, exaggerate the effects of hypotensive stress. It seems clear, however, that in the collateral zone where autoregulatory capacity to diminished perfusion pressure still shows appreciable impairment, increased perfusion pressure to increased systemic pressure is maintained, whereas in the most densely ischemic regions with flow less than 20% of control, autoregulation to both vasoconstrictor and vasodilator stimuli is effectively lost. This suggests that the ischemic damage to the nervous system in such extremely low-flow areas is accompanied by vasoparalysis in the area, with the establishment of a truly pressure-passive circulation.

The finding in the present experiments that the area of reduced perfusion produced by middle cerebral occlusion was peculiarly at risk when the circulation was stressed by further reduction of systemic blood pressure is of great significance in the clinical handling of problems such as aneurysm surgery. In the current studies, perceptible patchy pallor of areas of the cortex was apparent in the extreme hypotension of hemorrhage, as has been pointed out in other studies. 

References

2. Fog M: Cerebral circulation II. Reaction of pial arteries to increase in blood pressure. Arch Neurol Psychiat 41: 260-268, 1939
EEG Surveillance as a Means of Extending Operability in High Risk Carotid Endarterectomy

G. H. Matsumoto, M.D., J. D. Baker, M.D., C. W. Watson, M.D., B. Gleucklich, M.D., and A. D. Callow, M.D.

SUMMARY Some patients who have transient ischemic attacks are denied operation because severe occlusive lesions in other extracranial arteries may be inappropriately interpreted as constituting an unacceptable surgical risk, or because the lesion is so distal as to make its removal hazardous. Failure of endarterectomy is usually due to incomplete removal of the lesion or to thrombosis upon the frayed intima. Such lesions require excellent visualization and meticulous surgical technique — not always possible with a shunt. Among 130 consecutive carotid endarterectomies performed under general anesthesia, EEG changes consistent with cerebral ischemia appeared in only nine (7%). These patients required a shunt. In 11 patients normal EEG tracings were obtained during endarterectomy despite contralateral carotid occlusion. None of these patients had a neurological deficit. Continuous EEG monitoring is a reliable method of detecting changes in cerebral perfusion, permits a more meticulous endarterectomy in high-lying lesions without a shunt, and extends operability in high risk patients. Angiographical findings may be an unreliable predictor concerning risk of endarterectomy.

Introduction

CAROTID ENDARTERECTOMY for cerebrovascular insufficiency secondary to stenosis and emboli from an ulcerated atherosclerotic plaque in the extracranial internal carotid artery is a widely accepted mode of treatment. However, the methods of detection and the prevention of cerebral ischemia during endarterectomy are somewhat controversial.

Many measures to lessen the risk of carotid endarterectomy have been proposed. Regional anesthesia permits the patient's mental status to be monitored.

Increased cerebral blood flow is alleged to occur under general anesthesia. Hypercarbic general anesthesia has been proposed as a means of cerebral protection, but Boysen indicates there may be disturbances in regional cerebral blood flow although total cerebral blood flow may be increased. Routine use of an intraluminal shunt has been advocated. The insertion of a shunt may cause intimal damage and its presence may make the distal portion of the endarterectomy difficult. Cerebral embolism with a shunt in place has been reported. Because of these liabilities, some authors advocate the use of a shunt only when there is evidence of cerebral ischemia. Internal carotid back pressure has been used as an indicator of cerebral perfusion, but xenon flow studies indicate a poor relationship between back pressure and cerebral blood flow. Induced systemic hypertension increases cerebral blood flow and is used in conjunction with measurement of internal carotid back pressure. There is no agreement on the minimum pressure that is needed to protect against ischemia. Continuous EEG monitoring is utilized in this series as well as others. It can be used with general anesthesia. Studies show that left or right cerebral hypoperfusion will be detected on EEG.

In an attempt to identify those patients at high risk of incurring intraoperative cerebral ischemia or postoperative thrombosis, three potential high risk situations are investigated: (1) those patients with absent extracranial collateral vessels, (2) those with absent intracranial collateral vessels, and (3) those in whom postoperative internal carotid thrombosis or embolus, the distally extending lesion, is most likely to develop.

At the Eighth Conference of Cerebral Vascular Diseases, it was suggested that the risk of carotid surgery depended on coexisting cerebrovascular disease. At particularly high risk are those patients with stenosis of one carotid artery and occlusion of the other: 56 patients studied had an operative mortality of 16%. Another potential high risk group are patients in whom there is lack of arteriographic demonstration of intracerebral communicating vessels (anterior communicating or either posterior communicating artery). If these vessels are either absent or stenosed, localized ischemia may occur upon carotid cross clamping. We would like to define a third high risk group: patients whose lesion extends high into the extracranial internal carotid artery.
Autoregulation in acute focal ischemia. An experimental study.
L Symon, N M Branston and A J Strong

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