the widely patent ICA may have accounted for the eye bruit.

The results of the present study serve to re-emphasize that cervical and ocular bruits, identified by standard auscultation, are strongly associated with extracranial carotid occlusive disease.

Acknowledgment

We are grateful to J. P. Mohr, M.D., for his assistance in reviewing the manuscript.

References


Effects of Vasoconstriction and Distal Dilation on Carotid Stenoses in the Dog

WILLIAM P. SANTAMORE, PH.D.,* JAMES H. WOOD, M.D.,† ALFRED A. BOVE, M.D., PH.D.,‡ AND PABLO M. LAWNER, M.D.§

SUMMARY Traditionally, arterial stenoses have been assumed to be inflexible, static obstructive lesions that could not acutely change their configuration or cross-sectional area. However, recent clinical and experimental observations have shown that coronary arterial stenoses can respond to vasoconstriction and intraluminal pressure changes. This experimental study evaluated whether similar dynamic changes could occur in a carotid artery stenosis. The effects of dilation distal to a circumferential snare were examined in 6 mongrel dogs. To eliminate collateral flow, the distal carotid artery was occluded and blood flow diverted through a 16 or 20 gauge needle. With no stenosis, distal dilation increased flow from 29.0 ± 2.0 to 90.1 ± 3.8 ml/min, (p < 0.01). With moderate stenosis, the flow increase (25.5 ± 1.3 to 56.4 ± 3.7 ml/min, p < 0.01) following dilation was attenuated. With severe stenosis, flow paradoxically decreased (20.4 ± 1.0 to 11.4 ± 1.0 ml/min, p < 0.01). This flow decrease was associated with a large stenotic resistance increase (2.13 ± 0.51 to 18.93 ± 5.58 mm Hg/ml-min⁻¹, (p < 0.01). In eight additional experiments, an in vitro preparation was used to examine the effects of vasoconstriction on stenotic severity. Vasoconstriction, induced by ergonovine, methoxamine, angiotensin, or vasopressin, resulted in a significant flow decrease and stenotic resistance increase. Thus, both vasoconstriction and intraluminal pressure were shown to affect stenotic severity, and thereby influence blood flow. These data illustrate hemodynamic factors which may be important in patients with severe carotid artery stenosis.

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TRADITIONALLY, ARTERIAL STENOSES have been assumed to be inflexible, static lesions that could not acutely alter their configuration or cross-sectional area. However, recent clinical and experimental observations⁷, ¹³–¹⁸ of the coronary circulation have questioned this assumption. Coronary arterial stenoses have been shown to respond to vasoconstriction and changes in intraluminal pressure. The effects of dynamic stenoses on the coronary circulation provide a basis for understanding the clinical manifestations of coronary disease, and the observations raise questions concerning similar stenotic effects on the cerebral circulation. This experimental study applied concepts developed from the coronary circulation to evaluate whether similar dynamic changes could occur in extracranial carotid artery stenoses.

Methods

Effects of Distal Dilation

Six mongrel dogs (12.3–16.7 kg) were anesthetized with sodium pentobarbital (30 mg/kg) with supplemental doses as needed. The dogs were given 1,000 units sodium heparin. Via the left femoral artery, a
polyethylene catheter was inserted into the ascending aorta to measure aortic pressure. The left common carotid artery was exposed and an electromagnetic flow probe (Biotronex, Silver springs, MD) was placed around the artery. A snare occluder was placed around the carotid artery distal to the flow probe. The snare consisted of a 1–0 silk suture passed around the artery and through stiff polyethylene tubing. Varying degrees of constriction could be obtained by pulling the free ends of the silk suture. Distal to the snare occluder, a polyethylene catheter was inserted into the lingual artery and advanced into the left common carotid artery distal to the snare (see fig. 1a). The distal external and internal carotid arteries were ligated. Blood then flowed through the left carotid artery, passed the flow probe and snare, into the polyethylene catheter and either through a 20 gauge Longdwel needle (high distal resistance) or a 16 gauge Longdwel needle (low distal resistance). The blood was collected in a beaker and returned to the animal via an intravenous infusion. The carotid arterial pressure distal to the snare but proximal to the Longdwel needles was also measured. Aortic pressure, carotid blood flow and carotid arterial pressure were recorded on a physiologic recorder (Electronics for Medicine, Model DR-8, White Plains, NY).

Using this preparation, the effects of lowering the distal resistance on the flow through and pressure across the carotid stenosis were evaluated. With the blood flowing through the 20 gauge Longdwel needle (high distal resistance), various stenotic pressure gradients were created by progressively tightening the snare occluder. These stenotic pressure gradients (mean aortic pressure minus mean distal carotid artery pressure) ranged from zero (no constriction) to 50 mm Hg (severe partial occlusion). At each stenotic pressure gradient examined, the distal resistance was lowered by switching the stopcock to allow blood flow through the 16 gauge Longdwel needle. After recording the response, the stopcock was switched back reestablishing blood flow through the 20 gauge Longdwel needle. If the flow and pressure values varied more than 5% from controls, the data were discarded. The above procedure was repeated 10 to 20 times on each artery studied.

**Effects of Arterial Vasoconstriction**

In another set of experiments, the effects of arterial vasoconstriction on stenotic hemodynamics were examined in an *in vitro* carotid artery preparation. This preparation eliminated distal cerebral vasculature, neural, humoral, and systemic factors. Eight mongrel dogs (weighing 11.3 to 15.1 kilograms) were anesthetized with sodium pentobarbital (30 mg/kg) and their extracranial carotid arteries were removed. After removal, the arteries were attached to the perfusion apparatus.

The perfusion apparatus (fig. 1b) consisted of two pressure reservoirs, an arterial bath, and fixed distal resistance. One reservoir contained a 5.0 mMK physiologic solution (composition in millimoles per liter: 122.0 NaCl, 25.0 NaHCO₃, 1.2 NaH₂PO₄, 1.2 MgSO₄, 5.0 KCl, 2.5 CaCl₂, and 10 pyruvic acid, pH = 7.42) while the other reservoir contained a 100 mMK solution (composition in millimoles per liter: 24 NaCl, 25 NaHCO₃, 1.2 NaH₂PO₄, 1.2 MgSO₄, 100 KCl, 2.5 CaCl₂, 10 pyruvic acid, pH = 7.42). The arterial bath was filled with 5.0 mMK physiologic salt solution. All solutions were maintained at 37°C and were equilibrated with a gaseous mixture of 95% O₂, 5% CO₂. The distal resistance was produced by a 20 gauge Longdwel needle. Pressures, proximal and distal to the arterial segment, were measured with pressure transducers. Perfusion flow was measured with an extracorporeal flow probe (Biotronex, Silver Springs, MD), calibrated by a timed collection in a graduated cylinder. The data were recorded on a multichannel physiologic recorder (Electronics for Medicine, model DR-8, White Plains, NY).

The carotid artery segments were placed in the bath solution, attached to points a and b (fig. 1b) and stretched to their *in vivo* length. The reservoir pressure was applied to the arterial segment and the artery was allowed to stabilize for two hours. The reservoir pressure and the arterial length were kept constant throughout the experiment.

Prior to creating the stenosis, the hemodynamic response to arterial vasoconstriction was examined. The distal stopcock was opened and the perfusate was al-
lowed to flow through the artery. The variables were recorded while the artery was perfused with the 5.0 mMK physiologic salt solution. After five minutes, the perfusate was switched to the 100 mMK salt solution and the variables were recorded. Changing from a 5.0 mMK solution to a 100 mMK solution causes consistent carotid artery vasoconstriction. After five minutes, the artery was reperfused with the 5.0 mMK physiologic salt solution, and the arterial bath solution was drained and was refilled with the 5.0 mMK physiologic salt solution.

Next, the response to arterial vasoconstriction in the presence of a stenosis was examined. Internal obstruction (fig. 1b) was achieved by a 3F Fogarty balloon catheter. The carotid arterial segment was perfused with the 5.0 mMK physiologic salt solution and the balloon was inflated to create a pressure gradient across the artery. Note that the maximum arterial diameter was determined by the perfusion pressure. Therefore, the balloon did not and could not have created a bulge in the artery while still allowing flow through the artery. The Fogarty balloon catheter was inflated with an acrylic solution which solidified within half hour (JB-4, Polysciences, Inc. Warrington, PA). The acrylic solution insured a fixed stable intraluminal obstruction. The variables were recorded for 30 minutes to verify stability and to allow the acrylic solution to solidify. The perfusate was switched to the 100 mMK salt solution and the variables were recorded for five minutes. Using a calibrated eye piece, the arterial diameter proximal and distal to the stenosis was measured. The artery was then reperfused with the 5.0 mMK salt solution, the arterial bath was drained and refilled with the 5.0 mMK physiologic salt solution. The above procedure, except for inflating the balloon, was repeated three times on each artery studied.

In 6 additional experiments, the effects of various vasoconstrictor agents were examined with the methods outlined above. With the artery perfused by the normal physiological salt solution and the Fogarty balloon catheter inflated with the acrylic solution, various vasoconstrictor agents were added to the arterial bath solution. The pressure and flow response were recorded. The vasoconstrictor agents and their concentrations in the arterial bath were as follows: methoxamine (80 \( \mu \)M), ergonovine (4.5 \( \mu \)M), angiotension (7.6 \( \mu \)M), and vasopressin (2 U/L).

Data Analysis and Statistics

The stenotic resistance was calculated as the pressure gradient across the stenosis divided by the flow through the stenosis, the pressure gradient being the proximal (aortic) pressure minus the distal (carotid) pressure. The distal resistance was calculated as the distal pressure divided by the flow. The stenotic and distal resistances were only calculated when the flow was greater than 1.0 ml/min. In each data group, the mean and the standard error of the mean were determined for the aortic pressure, carotid arterial pressure, proximal pressure, distal pressure, flow, stenotic resistance, and distal resistance. For the vasoconstriction experiments, statistical significance was determined by comparing the 5.0 mMK response to the 100 mMK response by the Student’s \( t \) test or by comparing the measured variables before and after adding a vasoconstrictor agent to the arterial bath solution. For the distal dilation experiments, statistical analysis was performed by comparing the variables obtained with the high distal resistance to the variables recorded with the low distal resistance. Employing the paired two-tailed Student’s \( t \) test, significance was assumed when \( p < 0.05 \).

Results

Figures 2a, b, c, d and e are plots of aortic pressure, carotid pressure, and flow versus time. Figure 2a shows the typical responses obtained without partial arterial constriction. At the arrows, the distal resistance was either raised or lowered. As expected, lowering the distal resistance caused a large flow increase. The snare was then tightened to create a pressure gradient. With mild stenosis (fig. 2b), the pressure gradient, (aortic-carotid pressure) and flow increased following the distal resistance decrease. However, the flow increase was greatly attenuated. With further constriction (fig. 2c), flow remained unaltered as the distal resistance decreased, even though the pressure gradient across the stenosis increased. With still further constriction (fig. 2d), flow paradoxically decreased as the distal resistance decreased and flow increased as the distal resistance increased. With severe initial stenosis, the flow decrease, following dilation, could not be reversed by reestablishing the initial distal resistance. A typical example of this response is shown in figure 2e; however, this response is not included in the data table as previously described (since the variables changed by more than 5% from control and since the calculated stenotic resistance would be almost infinite with near zero flow).

Table 1 summarizes the results of the 6 experiments and is based upon 92 observations. The data were divided into four groups, as determined by their flow response to the distal resistance decrease. With no constriction, lowering the distal resistance always caused a large flow increase. With mild constriction, reducing the distal resistance increased flow, decreased carotid pressure and increased stenotic resistance. The flow increase, following dilation, was partially attenuated by the stenotic resistance increase. With further snare constriction, the flow remained almost unaltered following dilation. Carotid pressure fell and stenotic resistance increased greatly. The distal resistance decrease being notified by the stenotic resistance increase. Associated with these changes, there was a large distal carotid arterial pressure decrease. With severe initial stenosis, flow paradoxically decreased following dilation. Carotid pressure decreased and stenotic resistance increased. The flow decrease was partially due to the large stenotic resistance increase.

The effects of carotid artery vasoconstriction on pressure and flow in a stenosis that was created with an
intraluminal Fogarty balloon catheter are demonstrated in figure 3. With a 5.0 mM K physiologic salt solution perfusing the artery, the initial stenosis was established and was allowed to stabilize for 30 minutes. The perfusate was then switched to a 100 mM K salt solution. As observed in figure 3, arterial vasoconstriction severely reduced the flow through and increased the pressure across the stenosis. Thus, stenoses were extremely sensitive to arterial vasoconstriction.

The results from the eight carotid arteries studied are listed in table 2 and are based upon eight observations with no constriction, and 24 observations with an internal obstruction. Prior to the creation of an arterial stenosis, vasoconstriction had no significant effect on the measured and calculated variables. In striking contrast, with the stenosis produced by an intraluminal balloon catheter, arterial vasoconstriction caused significant hemodynamic changes. Distal pressure, flow, and distal diameter decreased and the stenotic resistance increased markedly. Thus, internal obstruction potentiated the effects of arterial vasoconstriction, causing significant hemodynamic changes. Vasoconstriction, induced by ergonovine, methoxamine, angiotensin, or vasopressin, caused a similar flow de-
TABLE 1  Hemodynamic Effects of Distal Dilation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Aortic pressure (mm Hg)</th>
<th>Carotid pressure (mm Hg)</th>
<th>Flow (ml/min)</th>
<th>Distal resistance (mm Hg/ml min⁻¹)</th>
<th>Stenotic resistance (mm Hg/ml min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No constriction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>high DR</td>
<td>129.0 ± 4.5</td>
<td>125.0 ± 4.7</td>
<td>29.0 ± 2.0</td>
<td>4.85 ± 0.34</td>
<td>—</td>
</tr>
<tr>
<td>low DR</td>
<td>126.0 ± 4.1</td>
<td>112.0 ± 4.4</td>
<td>90.1 ± 3.8*</td>
<td>1.33 ± 0.08*</td>
<td>—</td>
</tr>
<tr>
<td>Partial constriction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>high DR</td>
<td>123.5 ± 3.7</td>
<td>110.0 ± 4.2</td>
<td>25.5 ± 1.3</td>
<td>4.56 ± 0.23</td>
<td>0.65 ± 0.09</td>
</tr>
<tr>
<td>low DR</td>
<td>125.8 ± 2.6</td>
<td>60.3 ± 5.7*</td>
<td>56.4 ± 3.7*</td>
<td>1.16 ± 0.07*</td>
<td>1.77 ± 0.22*</td>
</tr>
<tr>
<td>Partial constriction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>minimal flow changes</td>
<td>high DR</td>
<td>122.4 ± 2.7</td>
<td>88.6 ± 5.5</td>
<td>20.6 ± 1.1</td>
<td>1.63 ± 0.22</td>
</tr>
<tr>
<td>low DR</td>
<td>121.3 ± 2.5</td>
<td>12.6 ± 2.9*</td>
<td>20.3 ± 1.2</td>
<td>0.60 ± 0.09*</td>
<td>5.63 ± 0.35*</td>
</tr>
<tr>
<td>Partial constriction</td>
<td>decrease flow</td>
<td>high DR</td>
<td>125.3 ± 2.4</td>
<td>80.3 ± 3.6</td>
<td>20.4 ± 1.0</td>
</tr>
<tr>
<td>low DR</td>
<td>125.5 ± 2.4</td>
<td>9.7 ± 2.7*</td>
<td>11.4 ± 1.0*</td>
<td>0.26 ± 0.06*</td>
<td>18.93 ± 5.58*</td>
</tr>
</tbody>
</table>

All data values mean ± standard error of mean.

*p < 0.05 as compared to high distal resistance valve by student’s t test.
Abbreviation: DR = distal resistance.

crease through the stenosis and pressure gradient increase across the stenosis.

Discussion

This experimental study examined the effects of intraluminal pressure and vasoconstriction on an animal model of carotid arterial stenosis. Reducing the resistance distal to the stenosis caused an increased pressure gradient across the stenosis and an increased stenotic resistance. In the presence of a severe stenosis, flow paradoxically decreased following a reduction in distal resistance. This paradoxical flow response was associated with a large stenotic resistance increase. In addition to changes in intraluminal pressure, vasoconstriction by the stenosis caused a decreased flow and increased pressure gradient across the stenosis. Without an underlying stenosis, vasoconstriction was ineffective in altering flow through the vessel. Thus, both vasoconstriction and intraluminal pressure were shown to alter carotid stenotic severity, similar to the clinical

TABLE 2  Hemodynamic Effects of Carotid Artery Vasoconstriction

<table>
<thead>
<tr>
<th>Condition</th>
<th>Distal pressure (mm Hg)</th>
<th>Flow (ml/min)</th>
<th>Stenotic resistance (mm Hg/ml·min⁻¹)</th>
<th>Proximal diameter (mm)</th>
<th>Distal diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.0 mMK</td>
<td>119.00 ± 2.58</td>
<td>35.77 ± 2.59</td>
<td></td>
<td></td>
<td>3.90 ± 1.07</td>
</tr>
<tr>
<td>100 mMK</td>
<td>119.39 ± 1.12</td>
<td>35.77 ± 2.47</td>
<td></td>
<td></td>
<td>3.98 ± 0.23</td>
</tr>
<tr>
<td>Internal obstruction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.0 mMK</td>
<td>94.70 ± 2.94</td>
<td>32.32 ± 0.75</td>
<td>0.96 ± 0.14</td>
<td>4.58 ± 0.08</td>
<td>4.04 ± 0.06</td>
</tr>
<tr>
<td>100 mMK</td>
<td>25.70 ± 4.91*</td>
<td>10.67 ± 1.67*</td>
<td>68.99 ± 14.09*</td>
<td>4.45 ± 0.09</td>
<td>3.18 ± 0.10*</td>
</tr>
<tr>
<td>Ergonovine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>before</td>
<td>79.88 ± 8.39</td>
<td>24.09 ± 1.51</td>
<td>1.93 ± 0.55</td>
<td>4.93 ± 0.32</td>
<td>4.63 ± 0.20</td>
</tr>
<tr>
<td>after</td>
<td>22.68 ± 14.77*</td>
<td>8.88 ± 3.46*</td>
<td>28.68 ± 8.44*</td>
<td>4.90 ± 0.30</td>
<td>4.03 ± 0.09*</td>
</tr>
<tr>
<td>Methoxamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>before</td>
<td>82.39 ± 7.32</td>
<td>23.94 ± 1.29</td>
<td>1.59 ± 0.27</td>
<td>4.98 ± 0.24</td>
<td>4.74 ± 0.21</td>
</tr>
<tr>
<td>after</td>
<td>36.40 ± 11.88*</td>
<td>13.56 ± 2.98*</td>
<td>12.73 ± 5.82*</td>
<td>4.96 ± 0.23</td>
<td>4.28 ± 0.24</td>
</tr>
<tr>
<td>Angiotensin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>before</td>
<td>94.47 ± 7.67</td>
<td>23.03 ± 0.58</td>
<td>1.21 ± 0.18</td>
<td>4.75 ± 0.45</td>
<td>4.65 ± 0.35</td>
</tr>
<tr>
<td>after</td>
<td>18.63 ± 19.29*</td>
<td>5.60 ± 5.35*</td>
<td>34.69 ± 15.31*</td>
<td>4.50 ± 0.50</td>
<td>2.75 ± 0.75*</td>
</tr>
<tr>
<td>Vasopressin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>before</td>
<td>75.16 ± 9.84</td>
<td>22.52 ± 1.83</td>
<td>1.93 ± 0.54</td>
<td>4.92 ± 0.29</td>
<td>4.58 ± 0.15</td>
</tr>
<tr>
<td>after</td>
<td>14.56 ± 11.84*</td>
<td>7.36 ± 2.87*</td>
<td>25.46 ± 10.17*</td>
<td>4.85 ± 0.26</td>
<td>3.30 ± 0.15*</td>
</tr>
</tbody>
</table>

All data values are mean ± standard error of mean.

*p < 0.05 by Student’s t test.
The mechanism by which intraluminal pressure and vasoconstriiction affect stenotic severity is probably a change in stenotic geometry. This premise is supported by the observed decreased flow through the stenosis with an increased pressure gradient across the stenosis. Only a stenotic geometric change could explain these data. With an underlying stenosis of 80 to 90% (as in this study), only a small further reduction in luminal cross-sectional area is required to cause a large reduction in flow.1, 8, 9 In the presence of a stenosis, distal dilation reduced the intraluminal pressure according to the Bernoulli principle. As blood flows through a stenosis, its potential energy (pressure) is converted to kinetic energy (increased velocity). At the outlet of the stenosis, part of the kinetic energy is converted back to potential energy (pressure) and part is lost due to flow turbulence. The pressure within the stenosis is therefore equal to or less than the distal pressure. In this study, distal dilation decreased carotid pressure, and therefore must have caused a decrease in intraluminal pressure by the stenosis. In turn, this decreased intraluminal pressure may have decreased the vessel diameter. Carotid artery vasoconstriction directly decreased the vessel diameter. The vasoconstriction was probably aided by the Bernoulli principle; with a lower intraluminal pressure by the stenosis, the same vasoconstriction stimulus would result in a greater vessel shortening. Thus, two different stimuli, distal dilation and carotid vasoconstriction, both could have decreased the vessel diameter. With an underlying stenosis of 80% to 90%, these small changes in luminal area could greatly increase the hemodynamic severity of the stenosis, and thereby decrease flow.

In a previous study, an in vitro arterial preparation was used to analyze the stenotic geometry changes that occurred after distal dilation.13 Microangiographic techniques were employed to measure the vessel diameter at the stenosis. Distal dilation increased stenotic resistance and decreased flow through the stenosed vessel. The distal dilation, by reducing intraluminal pressure, caused a decrease in stenotic luminal cross-sectional area. The change in stenotic geometry partially explained the increase in stenotic resistance.13 We would speculate that the observed stenotic resistance increases in this study after distal dilation or carotid artery vasoconstriction were also partially caused by a decrease in stenosis area.

For the experiments on the effects of distal dilation, the distal carotid artery was ligated and the blood flowed through either a 16 or 20 gauge Longdwell needle. This experimental preparation was employed in order to circumvent the extensive collateral circulation. In the normal canine, total ligation of a carotid artery results in little, if any decrease in the mean arterial pressure (distal to the ligation). Ligating both carotid arteries reduces mean distal arterial pressure only a few mm Hg. However, for the effects of distal dilation on stenotic severity to be observed, the carotid pressure, distal to the stenosis, has to have the potential to be lowered dramatically. Thus, the experimental preparation used in this study eliminated any potential collateral effects, thereby allowing a large range in distal carotid artery pressures.

The results of this study are only relevant to patients with high grade cerebral lesions, 80 to 90% reduction in luminal area. Further, for the arterial stenosis to respond to intraluminal pressure and vasoconstriction, a portion of the arterial wall by the stenosis must be normal.14-17 Several pathological studies indicate that many carotid and cerebral lesions are eccentric.5, 6 Kikuchi et al4 examined postmortem 423 human intracranial cerebral arteries. Most of the arterial lesions were eccentrically positioned. The atherosclerotic plaques were primarily located at the inner curvature at the terminal portion of the internal carotid artery, the median portion at the origin of the anterior cerebral artery, and the posterior portion at the origin of the posterior cerebral artery. Deweese et al18 studied 61 carotid arteries from patients undergoing carotid endarterectomy. The atherosclerotic plaques were eccentrically positioned in the carotid artery. Several types of lesions were noted. One type of lesion filled the bulb of the internal carotid artery with a smooth elliptical encroachment on the lumen. Other types produced bar- and diaphragm-like defects on the lumen. These anatomical studies5-8, 18 demonstrate that in some arterial stenosis part of the arterial wall is normal by the atherosclerotic plaque and conceivably able to respond to vasoconstriction and changes in intraluminal pressure. If the arterial lesion is concentric with a completely calcified lesion surrounding the remaining lumen, the arterial lesion will be nonresponsive to intraluminal pressure and vasoconstriction. Lastly, for the stenosis to respond to intraluminal pressure and vasoconstriction, there must be insufficient collateralization distal to the arterial lesion.

Clinically, the experience with cerebral vasodilators5, 6, 10, 11 has been disappointing. In the presence of arterial stenoses, cerebral vasodilatation and hypcapnia have been reported to cause either no change or a reduction in cerebral blood flow. Conversely, hypcapnia has been associated with an increased blood flow in patients with severe arterial stenosis.12 The results of these studies may help to explain these paradoxical responses. Distal dilation was associated with increased stenotic severity and a blood flow decrease, while increased distal resistance decreased stenotic severity with a possible blood flow increase. This inverse relationship between stenotic severity and intraluminal pressure may potentially help to explain the clinical results with cerebral vasodilators. Additionally, in this study, vasoconstriction by the stenosis was shown to increase stenotic severity and decrease flow through the artery. Conceivably, the cerebral vasodilators act primarily on the arterioles to induce vasodilatation and are not effective in dilating the larger arteries and collaterals. Thus, if the cerebral ischemia was due to vasoconstriction by the arterial lesions, many of the cerebral vasodilators would be ineffective. This may be analogous to the coronary circulation where nitro-
glycerin, a very effective anti-anginal agent, is weak distal coronary arteriolar vasodilator but a very potent dilator of the large coronary arteries and collaterals. While dipyridamole, an ineffective anti-anginal agent, is a potent distal coronary arteriolar vasodilator, but only a weak dilator of the large coronary arteries.

Although our study is compromised by the use of normal canine carotid arteries which differ markedly from those infiltrated with stenotic atherosclerotic plaques often found in patients with symptomatic cerebrovascular disease, our data illustrate hemodynamic factors that may influence blood flow to the brain in patients with carotid artery stenosis. Awareness of these potentially deleterious alterations affecting blood flow may explain the response to hypercapnia and pharmacologic cerebral vasodilators under conditions of cerebral ischemia.

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