Experimental augmentation of cerebral blood flow by intermittent aortic occlusion

FREDERICK A. SIMEONE, M.D., JOHN P. LAURENT, PETER J. TREPPER, DANIEL J. BROWN, AND JOHN COTTER
Department of Neurosurgery of the Pennsylvania Hospital and the University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Intermittent occlusion of the descending aorta just below the origin of the brachiocephalic vessels by a preformed balloon passed via the femoral artery is capable of significantly increasing the pressure and flow in the common carotid artery. Regional cerebral blood flow determination by the krypton-85 washout technique measured maximum increases of over 40% of the controls, which could easily be achieved and maintained. This technique apparently takes advantage of the finite delay in autoregulatory response to the increased arterial pressure before the onset of maximal autoregulation. Dogs were "pumped" in this way for up to 18 hours and survived in good health. Principal problems with this technique were the development of cerebral edema in the presence of diffuse established cerebral anoxia, and a shock-like cardiovascular response if the intermittent aortic occlusion was discontinued too abruptly. The clinical application of this technique to cerebral ischemia secondary to postoperative vasospasm may not require the extremes of hyperperfusion used in these experiments.

KEY WORDS: aortic occlusion · cerebral vasospasm · cerebral blood flow · cerebrovascular disease · common carotid artery · radiosotopes

No reliable method exists for increasing cerebral blood perfusion pressure over long periods of time. One possible use for increased cerebral perfusion pressure was suggested by Farhat and Schneider, who demonstrated alleviation of symptoms of cerebral ischemia in a patient with presumed cerebral vasospasm following aneurysm surgery. In this instance the authors induced marked systemic hypertension with pressor agents. Unfortunately, as they observed and we have confirmed, it is impossible to maintain high levels of systemic hypertension pharmacologically for more than a few hours. Apparently, depletion of endogenous catecholamine stores and receptor organ fatigue prevent sustained marked hypertension. The need for a safe, convenient, rapidly instituted technique for increasing cerebral perfusion pressure seems obvious and, in the laboratory, a variety of techniques were attempted. These were done in conjunction with an ongoing series of studies on experimental cerebral vasospasm in monkeys and dogs. Femoral-to-carotid shunts, external perfusion pumps, and various drugs proved either unsafe or ineffective. The method ultimately used consists of intermittent inflation of an occlusive polyurethane balloon high in the descending aorta, thereby forcing the cardiac output to the brachiocephalic vessels.

Materials and Methods

Initial Phase (Dogs)
For the initial phase of this series, 35 adult mongrel dogs weighing 40 to 50 lbs
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were used. They were anesthetized with intravenous sodium pentobarbital (25 mg/kg) intubated and maintained on controlled respiration with a Harvard respirator. Periodic blood pCO₂, pO₂, and pH measurements were made to ascertain respiratory stability. Central aortic blood pressure was measured through a right brachial arterial catheter and central venous pressure through a right brachial vein catheter, each by use of a Statham p 23 pressure transducer. Similarly, a polyethylene catheter was passed through a burr hole into the subdural space for the continuous measurement of intracranial pressure. Electromagnetic flow probes were placed about the right common carotid artery and right femoral or renal artery and connected to a Statham electromagnetic flow meter. These parameters plus an electrocardiogram were recorded on an eight-channel Grass polygraph. A Foley catheter was inserted for continuous measurement of urine volume and specific gravity. Serial hematocrits were taken throughout the experiment, and, when necessary, dog blood transfusions were administered. Renal clearance was tested by the phenolsulfonphthalein clearance method. Cardiac output, time tension index, cardiac work, etc., were also calculated during the experiment.

The occlusive balloon unit consists of an extracorporeal and intracorporeal component. The intracorporeal component is a preformed polyurethane balloon which, when fully expanded, achieves a maximum diameter of 1.5 cm. This balloon is identical to that used by Kantrowitz and co-workers as an auxiliary heart pump in cardiogenic shock. The balloon is inflated via a catheter approximately 50 cm long connected to the extracorporeal unit. With the aid of a stylet it is inserted into the left femoral artery and passed into the descending aorta to lie just distal to the left subclavian artery. The extracorporeal unit consists of an electronically controlled pump operated by solenoid valve and pressurized CO₂. Inflation of the balloon can be triggered by the R-wave of the electrocardiogram or the balloon can be paced independently for varying durations of inflation and deflation. The status of balloon inflation is marked automatically on the polygraph.

Initially, the balloon was paced on demand from the electrocardiogram. That is, with each R-wave the balloon would be inflated for varying duration then deflated until the next R-wave-instituted inflation. Later, the balloon was inflated for longer intervals and the effect of varying these intervals was noted. Similarly, various positions of the balloon in the descending aorta were studied. Figure 1 is a diagram of the experimental apparatus.

Fig. 1. Diagrammatic representation of physiological monitoring during intermittent aortic occlusion experiments.
Second Phase (Monkeys)

The second phase of the experiment was performed on 16 adult rhesus monkeys weighing from 5 to 12 kg. This animal was used because of the ease with which isotope washout curves can be recorded from the monkey's brain as well as the clarity with which angiograms can be performed on the monkey when altered states of cerebral perfusion, such as experimental cerebral vasospasm, are to be studied. The experiments on monkeys lasted up to 24 hours during which time the monkey was maintained under anesthesia. Anesthesia was induced and maintained with serial injections of phencyclidine (Sernylan),* a cataleptic agent which renders the animal unresponsive to pain but which preserves his pupillary and corneal reflexes. The animals were tracheostomized, paralyzed with curare, and maintained on controlled respiration via a Harvard respirator. The respiratory rate was determined by measurement of end-tidal pCO₂, through a Beckman gas sampling CO₂ analyzer with each respiration, complemented by serial arterial pCO₂, pO₂, and pH measurements. Blood gases were allowed to stabilize to normal levels prior to cerebral blood flow determinations. A rectal thermometer connected by a thermostat to a heat lamp automatically kept the animal's temperature constant to within ½°F. Blood pressure was recorded from a left brachial artery catheter passed into the aortic arch. A catheter passed into the right brachial artery under fluoroscopic control was positioned to lie at the root of the brachiocephalic vessels. An injection of radiopaque material into this catheter, when properly placed, would fill only the right common carotid and right vertebral arteries. Intracranial pressure was measured by a catheter threaded into the subdural space via a separate small burr hole. Blood pressure and intracranial pressure were recorded via Statham p 23A transducers.

A trephine hole was placed in the right temporal fossa along the course of the middle cerebral artery. The dura was opened in circular fashion with care to avoid trauma to the underlying brain, and a fitted radiolucent "washer" with a Mylar film stretched across its opening was screwed into the trephine opening. This produced a watertight seal that applied no pressure to the brain. After completion of surgery, 60 to 90 minutes were allowed for stabilization before cerebral blood flow records were begun. A 1 cm Geiger-Müller tube was placed 1 mm from the Mylar film. The preformed polyethylene balloon was inserted into the left femoral artery and passed under fluoroscopic control into the descending aorta, just distal to the left subclavian artery. The extracorporeal component was connected by a valve to this balloon. After control cerebral blood flow recordings were made, balloon pumping was performed usually in the ratio of 4 seconds of inflation to 1 second of deflation.

The isotope used was krypton 85, 10 mCi dissolved in 11 cc of saline. Approximately 2 mCi were injected for each flow determination. The beta emission of krypton was detected through the 1 cm Geiger-Muller tube placed in the previously described Mylar washers over the right hemisphere. Occasionally the position of the injection catheter was changed so that an injection of isotope would reach both hemispheres. Regional flow recordings could then be made from the right and left cerebral hemispheres in the distribution of each middle cerebral artery. Before each washout curve was recorded, care was taken to keep the CO₂, O₂, hematocrit, temperature, and, where applicable, blood pressure at the control levels. No isotope recording was made within ½ hour after an injection of radiopaque contrast material for angiographic morphology. Because of the short penetrance of beta particles in the brain, the recordings were essentially made from the first 0.3 mm of the cerebral cortex. The washout curves obtained, therefore, were a reflection of flow in the gray matter only. The beta emission of the isotope was amplified and recorded on a strip chart recorder with a time constant of 0.5. The data were processed on an IBM 360–30 computer according to a curve-fitting program. This program, described elsewhere,7 has the capacity to fit the data handled logarithmically into a very fast component and a slower component, both of which are presumed to reflect a flow in the gray matter. The areas under the fastest and slower component are calculated automatically, and

* Supplied by Parke, Davis and Company, Detroit, Michigan.
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flow values for each of these components are given, as well as a mean blood flow value. The computer also generates an error matrix and chi-square deviation values to test the statistical accuracy of the data it is handling. Flow value was accepted if:

1. The chi-square = x, where x = a ± 2s,
   a = arithmetic mean of the chi-square,
   s = standard deviation
2. The standard error on the slow flow = y,
   where y = b ± s,
   b = arithmetic mean of the standard errors,
   s = standard deviation.

Results

Effect on Common Carotid Blood Flow

All these data with the exception of regional cerebral blood flow determinations resulted from experiments on dogs. Intermittent aortic occlusion (IAO) using the EKG's R-wave as the stimulus to inflation was initially attempted. Figure 2 shows that mean increases in common carotid pressure and flow could be achieved to only 10% above the control values. It was apparent that a longer duration of aortic occlusion was necessary before maximum increments and perfusion pressure and flow could be achieved. Figure 3 shows that for approximately 5 seconds of occlusion there was a continuing rise in common carotid artery flow and pressure as well as intracranial pressure. Subsequently, there was a gradual tapering off of the flow, and if sufficient time was allowed the flow and intracranial pressure returned to almost normal; this gradual reduction in flow was presumably due to autoregulation. The common carotid artery flow probe, however, measured flow to the vascular structures of the face and head as well as brain flow, and, for this reason, the effect of autoregulation was less apparent.

It seems appropriate to presume that the gradual reduction in common carotid flow is at least in part due to autoregulation of cerebral vessels since this phenomenon is less active in the facial structures supplied principally by external carotid artery. Longer intervals of constant inflation were not studied further because they produced radical reduction in renal output and flow.

The optimum interval of inflation and deflation which would achieve maximum increase in cerebral perfusion pressure and common carotid flow yet preserve renal function varied from dog to dog. Analysis of empiric variations showed a ratio of 4:1 of inflation to deflation which seemed to be most consistent for the dogs tested. This ratio was established by inflating the balloon until maximum common carotid flow and pressure were achieved. This required from 4 to 10 seconds (Fig. 4). At the point of maximum flow and pressure, the balloon was deflated until the carotid flow reached the control level. Then the balloon was reinflated for the prescribed interval. If the deflation interval was allowed to proceed longer, the carotid flow dropped compensatorily below normal. In this way carotid flow and pressure could be maintained above normal for several hours without adjusting the inflation-deflation intervals. Continuous intermittent aortic occlusion (IAO) was maintained with full recovery of the animal for up to 18 hours (Fig. 5). During this interval it was necessary to adjust the deflation and inflation interval occasionally, and slow “weaning” from the balloon was required to avoid declining blood pressure. Mean increases in common carotid flow of 50% to 75% were easily maintained.

Effect on Carotid Blood Pressure

In general, the carotid pressure, or central aortic pressure above the balloon, varied in parallel with the carotid blood flow. Maximum increases in mean blood pressure of 35% were achieved regularly. The parallel nature of common carotid electromagnetic flow recordings suggested that to measure blood pressure above the balloon alone would be sufficient to monitor the effect of aortic occlusion. Table 1 demonstrates serial changes in blood pressure and electromagnetic flow recordings as measured from the graphic representation in a typical animal.

Effect on Central Venous Pressure

Central venous pressure measurements showed the usual fluctuation with respiration and were not significantly altered by IAO. Figure 4 shows changes in central venous pressure with 4:1 inflation to deflation intervals of the intra-aortic balloon. Central venous pressure did not materially change...
over a long duration of intermittent aortic occlusion. This was presumptive evidence that continuous IAO did not result in acute heart failure. Postmortem examination of the heart and lungs similarly showed no evidence of pathological cardiac dilation or pulmonary edema.

**Effect on Cardiac Function**

At the onset of aortic occlusion there was a pronounced bradycardia presumably due to the carotid sinus reflex. This effect was abolished by atropine, the administration of which became routine during the experiment. Cardiac output and left ventricular work were calculated by the dye dilution technique (Table 1). The significant increase in both of these functions was in part artifactual. The dye, administered in the brachial artery and withdrawn from the brachial vein, recirculated rapidly because aortic occlusion excluded it from transit through the...
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Fig. 3. The upward deflection of the balloon marker indicates the duration of a prolonged (10 sec) inflation of the intra-aortic balloon. A gradual decrement in intracranial pressure and carotid blood flow occurs half way during this inflation, presumably due to cerebrovascular autoregulation.
Recording from the right carotid blood flowmeter magnified to show the progressive increment in carotid flow to a maximum point during balloon inflation. Central venous pressure does not significantly change with aortic occlusion.
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rest of the body. There was no readily available technique which could accurately assess these functions in the presence of IAO. The time-tension index was calculated by multiplying the mean systolic pressure by the duration of the systole and dividing the product by the number of heartbeats per minute. Although a rather crude measurement, this did indicate an increase in systolic stress on the heart by pumping against a partially occluded aorta. During this increased effort, however, there was also a marked increase

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**Fig. 5.** Intermittent aortic occlusion carried on at the optimum ratio of 8 seconds inflation to 2 seconds deflation. Intermittent aortic occlusion begins at the dark vertical line. Note that the right carotid artery blood flow is kept consistently above control levels.
TABLE 1
Cardiovascular effects of sustained intermittent aortic occlusion

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Sustained 60 min</th>
<th>Intermittent 120 min</th>
<th>Aortic 150 min</th>
<th>Occlusion 180 min</th>
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<tr>
<td>carotid blood pressure (mm Hg)</td>
<td>150/100</td>
<td>215/130</td>
<td>210/140</td>
<td>215/155</td>
<td>220/125</td>
</tr>
<tr>
<td>carotid blood flow (cc/min)</td>
<td>40</td>
<td>75/40</td>
<td>80/40</td>
<td>75/40</td>
<td>75/35</td>
</tr>
<tr>
<td>intracranial pressure (mm Hg)</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>femoral blood flow (cc/min)</td>
<td>25</td>
<td>0/30</td>
<td>0/33</td>
<td>0/36</td>
<td>0/40</td>
</tr>
<tr>
<td>cardiac output (l/min)</td>
<td>3.5</td>
<td>5.0</td>
<td>5.0</td>
<td>5.5</td>
<td>5.0</td>
</tr>
<tr>
<td>time tension index (mm Hg sec/beat)</td>
<td>15.0</td>
<td>28.0</td>
<td>29.0</td>
<td>29.0</td>
<td>25.0</td>
</tr>
<tr>
<td>left ventricular work (mm Hg 1/min)</td>
<td>4.1</td>
<td>7.9</td>
<td>8.1</td>
<td>8.7</td>
<td>7.8</td>
</tr>
<tr>
<td>mean percentage changes:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>systolic (%)</td>
<td></td>
<td>43</td>
<td>40</td>
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<td>diastolic (%)</td>
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<td>35</td>
<td>25</td>
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<tr>
<td>mean (%)</td>
<td></td>
<td>36</td>
<td>40</td>
<td>36</td>
<td>34</td>
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<tr>
<td>cardiac output (%)</td>
<td></td>
<td>43</td>
<td>43</td>
<td>57</td>
<td>43</td>
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<tr>
<td>time tension index (%)</td>
<td></td>
<td>86</td>
<td>87</td>
<td>87</td>
<td>86</td>
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</table>

* The carotid and femoral blood flow figures are reported as the highest level during inflation and the lowest level during deflation. Carotid blood pressure is reported at the peak of inflation. Calculations of the cardiac output, and therefore left ventricular work, are inaccurate because of the aortic occlusion.

in coronary artery perfusion because of the elevated diastolic pressure. This added nourishment in part protected the myocardium from the increased stress.

After a prolonged interval of IAO, a precipitous drop in blood pressure was routinely noted if the IAO was stopped suddenly. This could be partially avoided by gradual reduction in the inflation-deflation ratio prior to cessation of IAO. It could be avoided entirely by allowing periodic "rest periods" without IAO.

Effect on Intracranial Pressure

Intracranial pressure was recorded reliably throughout most of the experiments. Inflation and deflation were invariably associated with an appropriate rise and fall in intracranial pressure when maximum carotid flow and pressure recordings were also noted. In only one instance did the intracranial pressure rise to dangerous levels. This was in a dog who early in the experiment underwent a significant period of anoxia and whose brain had apparently lost the capacity to autoregulate. This animal succumbed after developing an extremely high intracranial pressure.

Effect on Kidney Function

Urinary output was measured continuously, and periodic phenolsulfonphthalein clearance tests were performed in a series of animals. Urinary output was noted to decrease somewhat during prolonged aortic occlusion. This decrement, however, was never significant with ordinary IAO. More acute assessment of renal clearance was determined by the photometric analysis of blood and urinary phenolsulfonphthalein after an intravenous injection of this substance at 5 mg/kg. Dilution curves in six animals showed that the rate of excretion of phenolsulfonphthalein was not significantly changed after prolonged IAO. Animals that survived in good health after periods of up to 18 hours of continuous IAO provided evidence that chronic renal changes were not induced by this procedure.

During initial experiments, electromagnetic flow probes were placed about the renal and femoral arteries. During inflation there was a significant reduction of renal artery flow virtually to zero. After deflation, however, there was a marked compensatory overshoot in renal blood flow, indicating that renal artery perfusion occurred principally...
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throughout the deflation intervals (Fig. 5). Figure 6 shows the lag in reduction of renal flow compared to femoral flow at the onset of aortic occlusion. The differential requirements of cerebral blood flow and renal blood flow were sufficient to permit transient exclusion of the kidneys from circulation, as compared to exclusion of the brain. In practice, one might provide for "protection" of the kidneys with mannitol, or pH adjustments, but these were not tried in our experiments.

Postmortem examination of the animals demonstrated no gross pathological alterations of the heart, kidneys, or brain as a result of IAO. After the technique of balloon placement was perfected, there was no evidence of aortic wall damage as a result of the inflation and deflation.

Effect on Regional Cerebral Blood Flow

Valid serial cerebral regional blood flow recordings by the krypton 85 washout technique were obtained in only nine of the 16 monkeys because of the rigid criteria of stability required to compare post-IAO recordings to a series of controls in the same animal. Initially, it was necessary to establish the stability of the isotope washout technique. There were no data available in the literature to indicate the variability of serial control cerebral blood flow determination for experiments lasting more than 4 hours. Calculations in 10 control experiments lasting up to 34 hours indicated that serial blood flow determinations in the same animal could have a significant coefficient of variation as calculated by dividing the average flow into the average standard deviation for a series of flow values and converting this figure into percentage. The results of these control studies will be reported elsewhere, but for the purposes of this paper a coefficient of variation of 13.1% could be expected in most of our experiments. An alteration of 26% when compared to the mean control, therefore, was significant to the 95% confidence level.

The coefficient of variation was aggregate less for the mean flow values than for fast or slow component determinations. The mean flow was used principally to analyze the effect of IAO.

Table 2 lists the results of a 5-hour continuous IAO experiment. Note that the flow increased promptly after the institution of IAO.

Table 2

<table>
<thead>
<tr>
<th>Run No.</th>
<th>Time (hrs:mins)</th>
<th>Mean Flow (cc/gm/min)</th>
<th>Percent of Control Average (1.264)</th>
<th>Fastest Component</th>
<th>Slow Component</th>
<th>Intracranial Pressure (mm Hg)</th>
<th>Blood Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0:00</td>
<td>1.235</td>
<td>-2.2</td>
<td>10.205</td>
<td>1.024</td>
<td>0.609</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>0:30</td>
<td>1.275</td>
<td>+0.8</td>
<td>9.475</td>
<td>0.931</td>
<td>0.578</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>0:40</td>
<td>1.253</td>
<td>-0.8</td>
<td>8.023</td>
<td>0.837</td>
<td>0.450</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>1:00</td>
<td>1.274</td>
<td>+0.7</td>
<td>7.158</td>
<td>0.521</td>
<td>0.500</td>
<td>28</td>
</tr>
<tr>
<td>5</td>
<td>1:30</td>
<td>1.285</td>
<td>+1.6</td>
<td>8.942</td>
<td>1.029</td>
<td>0.557</td>
<td>32</td>
</tr>
<tr>
<td>6</td>
<td>1:45 Begin Intermittent Aortic Occlusion</td>
<td></td>
<td></td>
<td>1:45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>2:15</td>
<td>1.430</td>
<td>+13.1</td>
<td>9.105</td>
<td>0.803</td>
<td>0.883</td>
<td>32</td>
</tr>
<tr>
<td>8</td>
<td>3:00</td>
<td>1.612</td>
<td>+27.5</td>
<td>12.070</td>
<td>1.485</td>
<td>1.039</td>
<td>33</td>
</tr>
<tr>
<td>9</td>
<td>4:00</td>
<td>1.681</td>
<td>+32.9</td>
<td>19.025</td>
<td>2.725</td>
<td>1.155</td>
<td>32</td>
</tr>
<tr>
<td>10</td>
<td>5:30</td>
<td>1.837</td>
<td>+45.3</td>
<td>9.705</td>
<td>1.130</td>
<td>1.373</td>
<td>33</td>
</tr>
<tr>
<td>11</td>
<td>5:45</td>
<td>1.834</td>
<td>+45.8</td>
<td>23.669</td>
<td>4.458</td>
<td>1.436</td>
<td>33</td>
</tr>
<tr>
<td>12</td>
<td>6:30</td>
<td>1.952</td>
<td>+54.4</td>
<td>11.473</td>
<td>0.705</td>
<td>0.879</td>
<td>32</td>
</tr>
<tr>
<td>13</td>
<td>6:35 Terminate Intermittent Aortic Occlusion</td>
<td></td>
<td></td>
<td>6:35</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Flow data as reported by computer includes correction for hemoglobin and lists standard deviation for fastest and slow component.

The average "weight" of the fast component (the percentage of the mean flow represented by the fastest component) was only 6.7%. Therefore, despite the variability of the fast component, it represents only a small fraction of the mean flow determination. In Runs 3, 4, and 13, however, the fastest component represented slightly over 10% of the mean flow.
Fig. 6. Comparison of electromagnetic flow recordings from the renal and femoral arteries during one cycle of inflation and deflation. The line marked "control" indicates a linear relationship at rest. During inflation the femoral flow drops abruptly but real flow is maintained until near occlusion. During deflation renal flow recovers more slowly than femoral flow, but both overshoot control levels.

IAO. There was a steady increase in cerebral blood flow throughout the 5 hours during which IAO proceeded. Peak flows were usually reached in 3 to 5 hours, after which further increased cerebral blood flow was not observed. After cessation of the IAO the flow tended to remain above normal for some time. This was a consistent finding in successful IAO experiments. It was not unusual for cerebral blood flow to be elevated for over 30 minutes after termination of a 2- to 3-hour course of IAO. The mechanism for this persistent increase in flow is not understood. All animals from which data were used seemed to maintain the capacity to autoregulate after cessation of IAO. Autoregulation was tested by increasing systemic blood pressure modestly with norepinephrine during which a regional cerebral blood flow determination was made. Failure of the mean flow to rise above the anticipated coefficient of variation of the determination at that time was considered presumptive evidence of autoregulation. In addition, absence of an increase in intracranial pressure during the height of the pharmacological hypertension was considered an on-the-spot crude test for intact autoregulation. Preservation of autoregulation by these tests was rarely clear-cut and became more nebulous with experience.3

Figure 7 is a composite graphic recording of a series of regional cerebral blood flow determinations during varying durations of IAO in four typical monkeys. Despite modest fluctuations which were within the expected temporal coefficient of variation, it was clear that as IAO continued, greater increase in regional cerebral blood flow could be expected. Table 3 summarizes the data from the nine valid experiments in this series.
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Complications

One complication of this technique was the development of a shock-like state when IAO was stopped abruptly: if the IAO proceeded for more than 2 to 3 hours, abrupt cessation produced a sustained decrement in systemic arterial pressure to potentially dangerous levels. This could be averted somewhat with gradual "weaning" of the animal from IAO by shortening of the inflation interval and lengthening of the deflation interval. The complication of intracranial pressure has already been described in a dog who was subjected to IAO following a significant period of anoxia. Elevation of intracranial pressure was a problem in some monkey experiments which lasted more than 12 hours. Postmortem examination of the brain demonstrated edema but no evidence of parenchymal hemorrhage. We must conclude, however, that this technique would be dangerous in a brain subjected to generalized anoxia or other causes of serious disruption of the blood-brain barrier.

Discussion

Carotid artery blood pressure and common carotid artery electromagnetic flow recordings have indicated that a significant and prolonged increase in these two parameters is possible with IAO. This can occur without damage to the organism even though elevation of intracranial pressure and modest overall diminution of renal blood flow does occur. There is an increase in the work load on the heart with sustained IAO but no evidence in our animals of heart failure. Further cardiac function studies were performed subsequent to recording regional cerebral blood flow, and the duration and timing of IAO was altered. Continuous IAO for over 18 hours has been accomplished with prolonged survival of the animal to his preoperative state of health.

Fig. 7. Effects of varying the duration of pumping on the regional cerebral blood flow in four valid intermittent aortic occlusion experiments tabulated graphically. The wavy vertical line indicates the beginning of the intermittent aortic occlusion, and the vertical arrows the termination. Despite the variability, it is clear that as intermittent aortic occlusion increases in duration the mean cerebral blood flow proportionately increases. In no animal did the mean cerebral blood flow exceed the highest recordings on this chart.
TABLE 3
Mean cerebral blood flow values from nine valid experiments reported as percentage increase over mean control values for each animal during continuous IAO at 1, 2, and 5 hours*

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>1 Hr</th>
<th>2 Hrs</th>
<th>5 Hrs</th>
<th>At Termination (time)</th>
</tr>
</thead>
<tbody>
<tr>
<td>805</td>
<td>+9</td>
<td>+22</td>
<td></td>
<td>+40 (7 hrs) (9.3%)</td>
</tr>
<tr>
<td>806</td>
<td>+10</td>
<td>+14</td>
<td></td>
<td>+45 (9 hrs) (11.8%)</td>
</tr>
<tr>
<td>808</td>
<td>+10</td>
<td>+21</td>
<td>+34</td>
<td></td>
</tr>
<tr>
<td>809</td>
<td>+21</td>
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<td>+25</td>
<td>+38</td>
<td></td>
</tr>
<tr>
<td>824</td>
<td>+15</td>
<td>+18</td>
<td>+40</td>
<td>+37 (12 hrs) (13.1%)</td>
</tr>
</tbody>
</table>

* Last column shows total duration of IAO and mean flow increment at that time with the appropriate coefficient of variation.

Electromagnetic flow recordings on the common carotid artery, as well as blood pressure recordings, are at best a crude measure of cerebral blood flow. As Yoshida, et al.,16 have demonstrated, however, electromagnetic flow recordings on the carotid artery can suggest changes in the cerebrovascular bed. Since the structures supplied by the external carotid system act rather passively to changes in pressure and flow, one might assume that the gradual reductions, after an initial increase, in blood pressure, blood flow, and intracranial pressure as the balloon is inflated for a long period of time are due to cerebrovascular autoregulation. Their experiments showed that in monkeys during occlusion of the descending aorta with a clamp there was a significant increase in internal carotid artery flow (most of the external carotid system was surgically excluded) for an interval of a few seconds, after which autoregulation gradually effected return toward control electromagnetic flow recordings. It is this finite delay in autoregulation which is of interest at this point. Apparently the healthy cerebrovascular bed is capable of accommodating significant increases in flow for a short interval, presumably a few seconds, prior to the onset of autoregulation. Our assumption is that by intermittent occlusion and relaxation of occlusion at appropriate intervals one may take advantage of this delay in autoregulation and thereby continuously maintain cerebral blood flow above normal.

Presumably, in the well-autoregulating brain, the effect on cerebral blood flow of increasing carotid artery pressure should be less than in an injured or nonautoregulating brain. With disordered autoregulation, as is expected in symptomatic postoperative cerebral vasospasm, the cerebrovascular bed responds more passively to changes in pressure and flow.3

In the presence of profound generalized (not localized) cerebral ischemia or other causes of loss of autoregulation in large portions of the brain, this technique could dangerously elevate intracranial pressure by increasing brain volume. This effect would be ultimately complicated by diffuse cerebral edema. In the focal ischemia typical of postoperative vasospasm, this problem should be controllable. The purpose of the technique, namely, increased perfusion pressure through spastic cerebral arteries following intracranial aneurysm surgery, may not require the maximum IAO effect. This is because the patient with symptomatic cerebral vasospasm will have maximal dilatation of the arterioles (resistance) in the area to be hyperperfused, despite proximal constriction of large arteries. The ability of IAO to increase perfusion in the surrounding normal vasculature is important. Unlike other techniques which increase cerebral blood flow, namely, vasodilators such as CO₂, increased cerebral perfusion pressure favors the non-autoregulating brain presumably without a "steal" to the healthy autoregulating vessels.14,15 This is
Intermittent aortic occlusion evidenced by increased perfusion even in the autoregulating vasculature. Presumably the extremes of hyperfusion tried in these experiments would not be required clinically, thus diminishing the threat of diffuse cerebral edema. Clinical monitoring of the patient's neurological status might afford the best index of the extent to which IAO should be continued.

A series of IAO experiments during experimental cerebral vasospasm is planned. The effect of various techniques to produce prolonged experimental cerebral vasospasm on regional cerebral blood flow must first be delineated.\textsuperscript{11,14}

References

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Supported by Grant NS-08680 from the National Institute of Neurological Diseases and Blindness, and a grant from the Allan Miller Neurosurgical Research Fund.


Address reprint requests to: Frederick A. Simeone, M.D., Pennsylvania Hospital, Eighth and Spruce Streets, Philadelphia, Pennsylvania 19107.