Circulatory and Renal Adjustments to Acute Femoral Arteriovenous Fistulas

By Q. R. Murphy, Jr., M.D., K. S. Gullinson, B.S., C. H. Kratovil, M.D., and J. Simoes e Silva, Jr., M.D.

This paper is concerned with the pattern of cardiorespiratory and renal changes produced by opening a systemic arteriovenous fistula. Flow through bilateral femoral arteriovenous fistulas averaged approximately 53 per cent of the control cardiac output. The rise in cardiac output elicited by the shunt averaged 51 per cent of the shunt flow. PAH clearances decreased 23 per cent in animals anesthetized with sodium pentobarbital, and 46 per cent in animals premedicated with morphine sulfate prior to administration of sodium pentobarbital. The per cent reduction in renal blood flow did not differ significantly from the per cent reduction in flow through the extrarenal systemic capillary beds.

The purpose of this study was to determine the pattern of cardiorespiratory and renal adjustments in intact animals, that appear after the opening of a peripherally located systemic arteriovenous fistula, in order to obtain data on the immediate changes for comparison with responses resulting from a chronic fistula.

Frank et al.1 have described immediate hemodynamic effects of opening and closing arteriovenous fistulas. Their experiments differ from ours in that the chest was open, cardiac outputs were measured by rotameter, and the fistulas involved the carotid arteries. An arteriovenous fistula which is so located that the brain and the pressoreceptors are beyond it would be expected to have different effects from one located between the femoral arteries and veins. As blood is shunted from the carotid sinuses, causing a local lowering of pressure and a decrease in flow through the medullary centers, more prominent compensatory reactions might be expected than from a shunt which has as its only direct effect the lowering of the peripheral resistance and the sequestration of a small amount of blood.

METHODS

The studies were performed on dogs ranging in weight from 10 to 30 Kg. Some animals were anesthetized with intravenous sodium pentobarbital (30 mg./Kg.) while others were anesthetized with 12 mg./Kg. sodium pentobarbital given intravenously after premedication with intramuscular morphine sulfate (3 mg./Kg.). Morphine was used for the purpose of obtaining lower heart rates in the control periods. A bilateral femoral arteriovenous fistula was established prior to the collection periods and the flow through it was measured by the recording rotameter of Shipley and Wilson.2 The inflow spout of the rotameter was connected to the femoral arteries and the outflow spout to the femoral veins. Mepesulfate (30 mg./Kg.) or heparin (10 u/w/Kg.) was given intravenously before the fistula was opened. The dogs were hydrated with intravenous infusions of 0.9 per cent sodium chloride solution or Ringer-Locke solution. Following a priming injection, sodium para-aminobipppurate (PAH) was infused intravenously at a rate adjusted to maintain an adequate urine production and a plasma PAH concentration in the range for clearance studies of renal blood flow. In each experiment there were one to three 20 minute collection periods before the fistula was opened, followed by a 20 minute collection period with the fistula open. Urine was collected by means of a urethral catheter and the bladder was rinsed with distilled water at the end of each collection. Blood samples for renal function analyses were taken at the midpoint of each collection period. Endogenous creatinine was determined by the method of Hare3 and PAH by the method of Smith et al.4 Cardiac outputs were determined by the Fick principle and arterial,

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right ventricular and expired air samples for these were collected simultaneously over the last 5 min. of both the final control and the shunt periods. The blood samples were analyzed for oxygen by the method of Van Slyke and Neill and expired air analyses were done on the Haldane apparatus. All analyses were made in duplicate.

RESULTS

Urine volumes, endogenous creatinine clearances and PAH clearances were measured for 7 consecutive 20 minute periods in 5 dogs anesthetized with sodium pentobarbital. The trend of the means was slightly upward and there were no statistically significant changes from one period to the next for either the individual or the mean changes in any of the measurements. The means and ranges from the 5 experiments are shown in figure 1.

Previously cardiac output was determined twice in each of 15 dogs anesthetized with sodium pentobarbital, by techniques similar to those used in our present experiments. Measurements obtained 30 minutes after the initial measurements showed the following mean changes: mean arterial blood pressure, +3 per cent; cardiac output, —9 per cent; heart rate, —3 per cent. None of these changes was statistically significant.

Cardiorespiratory Responses

Within a few seconds after the shunt was opened, typically a considerable decrease in arterial blood pressure occurred similar to that observed by Van Loo and Heringman, but this was largely counteracted within the first minute or two, presumably through cardiac stimulation and vasoconstriction. Following this transition, the heart rate and blood pressure leveled off and remained essentially as stable as in the control periods. The flow through the bilateral fistula also remained relatively constant for the individual animal after this initial adjustment phase.

Both cardiorespiratory and renal responses were studied in 6 animals anesthetized with morphine and pentobarbital. The fistula flows ranged from 1270 to 1740 ml./min. and amounted to 41 to 68 per cent of their respective preshunt cardiac outputs. The per cent compensation

\[
\frac{\text{fistula C.O. minus control C.O.}}{\text{fistula flow}} \times 100
\]

varied from 23 to 115 for this series. The other responses are shown in table 1.

Fourteen animals also anesthetized with morphine and pentobarbital received procaine in the groins to inhibit afferent influences arising as a result of the incisions and cannulae. Except for changes in mean arterial blood pressure and expired air volume, the cardiorespiratory adjustments elicited by opening the fistula were similar to those obtained in the animals which were not given procaine. The shunt flows in these dogs ranged from 940 to 1730 ml./min., representing from 22 to 83 per cent of their control cardiac outputs. Per cent compensation in this series varied from —8 to +108. The other changes obtained are listed in table 1.

Renal Responses

Animals Anesthetized with Sodium Pentobarbital. In 5 dogs with unilateral femoral fistulas, the mean changes in creatinine clearance (—14 per cent) and PAH clearance (—6

![Figure 1. Results of measurements of renal functions during consecutive 20 minute periods obtained from 5 dogs anesthetized with sodium pentobarbital. Closed circles represent the means and the connecting lines indicate the ranges.](http://circres.ahajournals.org/Downloaded from)
TABLE 1.— Changes in the Shunt Period Compared with the Preceding Control Period
(Mean Average Values)

<table>
<thead>
<tr>
<th>Fistula flow (mL/min.)</th>
<th>Fistula flow</th>
<th>Control cardiac output</th>
<th>Per cent compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control value (L/min.)</td>
<td>14.50</td>
<td>54.0</td>
<td>32.0</td>
</tr>
<tr>
<td>S.D. of individual differences</td>
<td>2.9</td>
<td>3.4</td>
<td>2.8</td>
</tr>
<tr>
<td>Change (%)</td>
<td>25.8*</td>
<td>4.5</td>
<td>27.4*</td>
</tr>
<tr>
<td>Cardiac output (L/min.)</td>
<td>11.55</td>
<td>26.5</td>
<td>117.8</td>
</tr>
<tr>
<td>S.D. of individual differences</td>
<td>11.6</td>
<td>4.1</td>
<td>11.75</td>
</tr>
<tr>
<td>Heart rate (beats/min.)</td>
<td>39.5</td>
<td>26.5</td>
<td>39.5</td>
</tr>
<tr>
<td>S.D. of individual differences</td>
<td>2.9</td>
<td>0.7</td>
<td>7.4</td>
</tr>
<tr>
<td>Stroke volume (mL.)</td>
<td>39.5</td>
<td>28.8</td>
<td>21.3</td>
</tr>
<tr>
<td>Mean arterial blood pressure (mm Hg)</td>
<td>2.8</td>
<td>2.4</td>
<td>2.8</td>
</tr>
<tr>
<td>Expired air volume (L/min.)</td>
<td>4.54</td>
<td>4.5</td>
<td>4.5</td>
</tr>
<tr>
<td>S.D. of individual differences</td>
<td>11.6</td>
<td>2.4</td>
<td>11.75</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>39.5</td>
<td>39.5</td>
<td>39.5</td>
</tr>
<tr>
<td>S.D. of individual differences</td>
<td>2.9</td>
<td>0.7</td>
<td>7.4</td>
</tr>
<tr>
<td>Urine volume (mL/min.)</td>
<td>148.0</td>
<td>21.3</td>
<td>21.3</td>
</tr>
<tr>
<td>S.D. of individual differences</td>
<td>11.6</td>
<td>2.4</td>
<td>11.75</td>
</tr>
<tr>
<td>Creatinine clearance (mL/min.)</td>
<td>117.8</td>
<td>117.8</td>
<td>117.8</td>
</tr>
<tr>
<td>PAH clearance (blood)</td>
<td>39.5</td>
<td>39.5</td>
<td>39.5</td>
</tr>
<tr>
<td>S.D. of individual differences</td>
<td>2.9</td>
<td>0.7</td>
<td>7.4</td>
</tr>
<tr>
<td>Plasma PAH clearance</td>
<td>39.5</td>
<td>39.5</td>
<td>39.5</td>
</tr>
<tr>
<td>S.D. of individual differences</td>
<td>2.9</td>
<td>0.7</td>
<td>7.4</td>
</tr>
</tbody>
</table>

*P = <.01, +P = <.05.
S.D. = standard deviation.

per cent) were not statistically significant. The shunt flow was not measured in this group but it may be assumed to be approximately one half the volume of the bilateral fistulas, or about 500 to 800 mL/min.

In 7 animals with bilateral fistulas, the only statistically significant change observed in response to opening the fistulas was a decrease in PAH clearance. PAH extraction ratios were done on some of these dogs, and although they varied from dog to dog, they were found to be relatively constant in the individual animal. Therefore, the per cent changes in creatinine clearance and PAH clearance (blood) may be taken as indices of per cent changes in glomerular filtration rate and renal blood flow respectively. Fistula flows and per cent compensations determined in 3 of these experiments were within the ranges observed in the other groups. In these 3 dogs, the average reduction in PAH clearance was 41 per cent, while the reduction in flow through the systemic circuit exclusive of the fistula was 39 per cent. The changes in renal function are presented in table 1.

Animals Anesthetized with Morphine Sulfate and Sodium Pentobarbital. In this group of 6 dogs there was a statistically significant decrease in urine volume and in PAH clearance and a statistically significant increase in the ratio of creatinine clearance to PAH clearance in response to opening the shunt. The considerable per cent decrease in PAH clearance with no significant change in creatinine clearance indicates that relatively preponderant efferent arteriolar constriction occurred. It is possible that this response is, in part, elicited reflexly from the pressoreceptors when the fistula is opened. In any case, this response was much greater when the dogs received morphine premedication. The average reduction in PAH clearance was 46 per cent, while the flow through the systemic capillary beds was reduced 28 per cent in this group. However, in two of the experiments the per cent reduction in systemic flow was...
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greater than the per cent reduction in PAH clearance. The changes are presented in table 1.

**DISCUSSION**

Since the increase in cardiac output, occurring under the conditions of these experiments, when a femoral arteriovenous fistula was opened, averaged about 51 per cent of the shunt flow, a deficit in blood flow through the capillary beds of the systemic circuit was produced. One reason for following the changes in renal clearances simultaneously with the cardiovascular responses was to determine whether or not the kidney shares proportionately in this circulatory deficit. With shunts of the size and location studied, the most prominent change in renal function was the decrease in blood flow, and when the per cent reduction in renal blood flow is compared with the per cent reduction in flow through the systemic capillary beds it is found that on the average they do not differ greatly.

The animals with femoral fistulas reported here showed a lesser per cent compensation relative to the size of the shunt flow than appears to have been the case in those studied by Frank et al. However, their control cardiac outputs, as measured by rotameter, were somewhat lower than generally obtained in dogs. Also, the fistulas in their studies were open only about 5 min and, from the examples given, downward trends in the cardiac outputs were observed; therefore, it is possible that lower per cent compensations might have been observed if the fistulas had been patent for a longer period of time. We did not obtain any correlation between the size of the fistula relative to the control cardiac output and the per cent compensation. However, the fistula flow volumes were rather large in our dogs and such a correlation may only be present when smaller fistula flows are established, as in the animals with unilateral femoral arteriovenous fistulas reported by Van Loo and Herlingman. Another difference between our results and those reported by Frank et al. is that the control heart rates were lower in our studies and showed a greater per cent increase in response to opening the shunt.

A paper by Hilton et al. describes the effects of systemic arteriovenous fistulas on renal functions. These fistulas also involved the carotid arteries. They reported moderate decreases in PAH and creatinine clearances. The magnitude of the effect of the shunts on PAH clearances tends to be greater in our studies in dogs with bilateral fistulas. Although the volumes of the shunt flows were not stated by Hilton et al., it is possible that they were comparatively small, since the percentage changes they reported are quite similar to those that we observed in dogs with unilateral femoral fistulas.

**SUMMARY**

Cardiovascular and renal adjustments immediately following the opening of a bilateral femoral arteriovenous fistula have been studied in anesthetized dogs. The volume of flow through the fistula averaged about 53 per cent of the control cardiac output. Cardiac output increased an average of 27 per cent, heart rate increased an average of 32 per cent and there was no consistent change in stroke volume. The increment by which the cardiac output increased on opening the fistula averaged 51 per cent of the shunt flow; therefore a deficit in body flow occurred.

On opening the fistula the urine volume decreased. PAH clearance decreased and creatinine clearance was not significantly changed. Since glomerular filtration rate remained relatively constant, efferent arteriolar constriction is indicated, and this was much greater when the animals were premedicated with morphine. There was no indication that the renal vascular bed shared disproportionately in the circulatory deficit.

**SUMMARIO IN INTERLINGUA**

Le adjustamentos cardiovascular e renal que occurre immediatamente post le activation de bilateral fistulas arterio-venose del femores eseva studiate in canes anesthesiata. Le volume medie del fluxo a transverso le fistula eseva circa 53 pro cento del rendimento cardiac de le canis.
de controllo. Esseva constatate un aumento medie de 27 pro cento in le rendimento cardiaco, un acceleration medie de 32 pro cento in le frequentia del corde, e nulle alteration uniforme in le volumine per pulso. Le augmento medie del rendimento cardiaco OCCurrente post le activation del fistulas esseva 51 pro cento del fluo in le derivation. Occurreva per consequente un deficit in le fluo corporee.

Post le activation del fistulas il habeva un reduction del volumine de urina, un diminution del clearance de acido para-aminohippuric, e nulle alteration significative del clearance de creatinina. Viste que le intensitate del filtration glomerular remaneva relativemente constante, on debe supponer que il habeva constriction arteriolar efferente. Isto esseva molto plus pronunciate quando le animali esseva premedicate con morphina. Esseva notate nulle indication que le vasculatura renal participava disproportionatamente in le deficit circulatori.

REFERENCES
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