Contribution of Baroreceptors to the Control of Renal Function

By Joseph P. Gilmore, M.S., Ph.D.

In experiments undertaken to produce acute hypertension by left stellate ganglion stimulation, it was observed that during such stimulation a diuresis occurred which was not related to changes in mean arterial pressure. In fact, diuresis was sometimes observed in animals in which mean arterial pressure remained the same or declined. During the diuresis, a decline in left atrial pressure was also observed. According to the atrial volume receptor hypothesis, a decline in left atrial pressure should decrease the rate of discharge in atrial afferent nerves and increase the secretion of the antidiuretic hormone and decrease urine flow. In view of these preliminary observations it appeared worthwhile to undertake more definitive experiments to determine the cause of the diuresis observed during stellate ganglion stimulation. The results of these experiments indicate that the diuresis is reflex in nature, the stimulus appearing to be the increase in arterial pulse pressure induced by stimulation of the cardiac sympathetic efferent nerves. This increase in pulse pressure presumably stimulates the baroreceptors, subsequent to which there occurs a reflex diminution of activity in the renal sympathetic efferent nerves. This in turn leads to an increase in glomerular filtration rate and water and electrolyte excretion.

During these experiments it was noted that little or no change in urine flow occurred when renal nerve activity was increased reflexly by carotid artery occlusion despite substantial increases in renal arterial blood pressure. This observation was of interest since there are several conflicting reports in the literature describing the response of urine flow to carotid artery occlusion. Further studies were therefore made to determine the effects of carotid artery occlusion on renal function and perhaps to discover the reasons for the conflicting results. In the early experiments it was observed that during carotid artery occlusion urine flow and electrolyte excretion did not always parallel the changes in renal plasma flow and glomerular filtration rate. Since both renal sympathetic nerve activity and renal arterial pressure increase during carotid artery occlusion it became apparent that in order to study the mechanisms concerned in the response of renal blood flow to carotid artery occlusion a preparation was required in which the influence of the one factor could be determined independently of changes in the other. To this end, an intact perfused kidney preparation was developed in which left renal blood flow could be monitored continuously. The results of the carotid occlusion study indicate that the effect on the kidney of lowering the carotid sinus pressure is the result of at least two effects; one direct and the other indirect. The direct effect is caused by the rise in renal arterial pressure; the indirect effect is caused by the reflex increase in renal vascular resistance. These data have been presented previously in abstract form.

Methods

GENERAL

Male and female mongrel dogs (11 to 23 kg), anesthetized with pentobarbital sodium (30 mg/kg), intravenously were used. The trachea was intubated, and the required blood vessels exposed. The carotid arteries and vagus nerves were exposed in the cervical region. Urine samples were obtained by direct catheterization of the ureters through a low midline abdominal incision, and the urine collected in gradua-
ed tubes. All infusions were given into a jugular vein by a calibrated pump. An infusion of 0.9% sodium chloride was given at a rate of approximately 0.1 ml/min/kg body wt, in those experiments in which renal clearance determinations were not done. In some experiments mannitol (5% in 50 mEq/liter NaCl) was infused to establish a diuresis. Blood samples were obtained from a femoral artery. Arterial blood pressure was measured through a metal cannula in a brachial or a femoral artery. Left atrial pressure was measured through a small branch of a pulmonary vein, or through a metal cannula inserted directly into the atrial appendage. Both arterial and atrial pressures were measured with Sanborn 267B differential transducers. All continuous recordings were made on a Sanborn multichannel oscillograph.

SPECIAL PROCEDURES
Stimulation of the Stellate Ganglion

The left chest was opened through the third intercostal space while maintaining intermittent positive pressure ventilation. The left stellate ganglion was isolated by sectioning all rami so that only the cardiac sympathetic outflow was intact. The ganglion was then placed in a shielded bipolar platinum electrode. The ganglion was stimulated using a square pulse stimulator at frequencies of three to six per second, at intensities of three to six volts and a duration of one millisecond.

Heart rate was maintained constant in some experiments by bipolar stimulation of the atrial appendage using a second Grass stimulator. Except where indicated otherwise, vagotomy was done by section of the cervical vagosympathetic trunk.

Perfused Kidney Preparation

The lower abdominal aorta was approached retroperitoneally through a left flank incision and the lumbar arteries ligated. The animal was then given 5 mg/kg of heparin intravenously and a Gregg coronary cannula, slightly modified by putting a metal flange on the tip, inserted into the aorta approximately 5 cm below the left renal artery. The kidney was perfused through this cannula from the right common carotid artery via a rotameter. The cannula was moved anteriorly and wedged into the left renal artery without interruption of blood flow. The kidney was not disturbed during the procedure, and the position of the cannula during the wedging determined by palpation. That size cannula was used which would fit tightly in the artery so that no ligature was necessary to hold it in place or prevent flow around it. Left renal arterial pressure was measured through a needle inserted into the renal perfusion line close to the aorta. In some experiments a roller pump was employed in the perfusion circuit between the carotid artery and the rotameter to maintain blood flow constant. In most experiments, however, renal blood flow was controlled by changing renal inflow resistance with a screw clamp placed on the renal inflow tubing. Kidney weight was obtained at the end of the experiment after excising the organ, clearing all tissue attached to the capsule, cutting the blood vessels and ureter close to the pelvis and then squeezing the kidney gently between absorbent paper. The essentials of the renal perfusion system are shown in figure 1.

CHEMICAL PROCEDURES

The renal clearance of para-amino hippuric acid (PAH) was used as a measure of renal plasma flow and the renal clearance of inulin as a measure of glomerular filtration rate. A priming injection of 15 mg/kg of inulin was given intravenously and then an intravenous sustaining infusion of 0.9% sodium chloride, containing approximately 5 mg/ml of inulin and 2 mg/ml of para-amino hippuric acid begun at a constant infusion rate of approximately 2 ml/10 kg body weight. After a 40- to 60-minute equilibrium period urine and blood samples were obtained. Urine samples were usually obtained every 10 minutes, and the arterial blood samples collected in heparinized tubes at the midpoints of the urine collection periods. When an experimental intervention was made, the first 5 ml of urine collected were usually discarded. Plasma and urine inulin was determined by the method of Walser et al. and PAH by the method of Bratton and Marshall. EPAH was not determined. Sodium and potassium were analyzed using a Patwin flame photometer, chloride using the instrument and method described by Cotlove et al., and osmolality by freezing point depression.

FIGURE 1
Perfused left kidney preparation. See text for description.
FIGURE 2
Experiment illustrating the effect of stellate ganglion stimulation on arterial pressure, heart rate, left atrial pressure, chloride and solute excretion and urine flow. AP = arterial pressure; upper line = systolic; middle line = mean; lower line = diastolic pressure. HR = heart rate. LAP = mean left atrial pressure. Cl− = urinary chloride excretion. Solutes = total urinary solute excretion. Stellate stimulation at 1 msec, 4 volts, 5/sec.

Stellate Ganglion Stimulation Results
Effects on Arterial Blood Pressure, Left Atrial Pressure, and Renal Function

Figure 2 shows some of the hemodynamic and renal responses to stimulation of the left stellate ganglion. During stimulation pulse pressure widened primarily as a result of an increase in systolic pressure while mean arterial pressure showed little change. With the increase in pulse pressure there was a decline in mean left atrial pressure and a substantial increase in urine flow, and chloride and solute excretion. The renal changes invariably began within one minute after the changes in arterial pressure occurred. With the cessation of stimulation, pressures and urine flow and elec-

FIGURE 3
Experiment illustrating the effect of stellate ganglion stimulation on electrolyte excretion. AP = arterial pressure; upper line = systolic; lower line = diastolic pressure. LAP = mean left atrial pressure. Osmolality = total urinary solute concentration. Solutes = total urinary solute excretion. U = urine. Stellate stimulation at 1 msec, 5 volts, 5/sec.
trolyte excretion usually returned to the prestimulation values. In this experiment heart rate changed little during stimulation. However, stellate ganglion stimulation was usually associated with a tachycardia. In each of the 33 dogs not receiving mannitol, left stellate ganglion stimulation was accompanied by an increase in urine flow, a widening of arterial pulse pressure and, when measured, a decline in mean left atrial pressure. Prior to stimulation urine flow averaged 0.58 ± 0.51 ml/min; during stimulation urine flow averaged 1.70 ± 1.08 ml/min.

The effect of stellate ganglion stimulation on urinary concentration and excretion of sodium, potassium, and total solutes is shown in figure 3. During stimulation the urinary concentration of total solutes and sodium declined but total excretion increased. However, potassium concentration fell to a greater extent so that during the second stimulation period total potassium excretion was not different from that in the control period. Estimated free water clearance increased slightly (—0.25 to —0.19 ml/min). In general, during stellate stimulation, sodium, chloride, and solute excretion increased substantially whereas potassium excretion showed minimal changes. Figure 4 shows a similar experiment done in a dog undergoing mannitol diuresis.

Stellate ganglion stimulation was accompanied by either no measurable change or an increase in inulin clearance (table 1). In gen-

---

**Figure 5**

Experiment illustrating the effect of vagotomy upon the diuretic response to stellate ganglion stimulation. AP = arterial pressure; upper line = systolic, middle line = mean, lower line = diastolic pressure. HR = heart rate. LAP = mean left atrial pressure. Vagotomy = bilateral cervical vagotomy. Carotid Occlus = bilateral carotid occlusion. All stellate stimulations at 1 msec, 3 volts, 5/sec.
TABLE 1

Effect of Left Stellate Ganglion Stimulation on Inulin Clearance

<table>
<thead>
<tr>
<th>Exp. no.</th>
<th>Dog wt kg</th>
<th>Urine vol ml/min</th>
<th>Control C\text{\textit{inulin}} ml/min</th>
<th>Stimulation Urine vol ml/min</th>
<th>Control C\text{\textit{inulin}} ml/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td>10.5</td>
<td>0.10</td>
<td>42.0</td>
<td>0.90</td>
<td>42.0</td>
</tr>
<tr>
<td>-2</td>
<td>12.0</td>
<td>0.15</td>
<td>20.5</td>
<td>3.25</td>
<td>39.2</td>
</tr>
<tr>
<td>-3</td>
<td>12.5</td>
<td>0.18</td>
<td>37.3</td>
<td>1.80</td>
<td>38.9</td>
</tr>
<tr>
<td>-4</td>
<td>13.5</td>
<td>0.43</td>
<td>37.6</td>
<td>0.90</td>
<td>33.0</td>
</tr>
<tr>
<td>-5</td>
<td>19.0</td>
<td>0.54</td>
<td>45.7</td>
<td>0.72</td>
<td>41.5</td>
</tr>
<tr>
<td>-6</td>
<td>12.5</td>
<td>0.32</td>
<td>30.4</td>
<td>1.82</td>
<td>32.7</td>
</tr>
<tr>
<td>-9</td>
<td>11.0</td>
<td>0.86</td>
<td>22.8</td>
<td>1.58</td>
<td>30.5</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>0.52</td>
<td>31.0</td>
<td>1.50</td>
<td>35.0</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td>0.28</td>
<td>9.5</td>
<td>0.73</td>
<td>5.4</td>
</tr>
</tbody>
</table>

eral, the higher the inulin clearance prior to stimulation the less was the change during stimulation. Also, the greater the change in clearance the greater was the increase in urine flow. However, even in those experiments in which stellate stimulation did not produce a measurable change in inulin clearance, an increase in urine flow was observed.

Effects of Vagotomy on the Responses to Stellate Ganglion Stimulation

Since it has been reported that the diuresis produced by left atrial distension is diminished by cervical vagotomy,1,3 experiments were undertaken to determine the effects of bilateral cervical vagotomy on the diuretic response to stellate ganglion stimulation. Figure 5 shows one such experiment. Prior to vagotomy, stellate stimulation produced a substantial increase in urine flow. The absence of a diuresis during carotid occlusion indicates that the increase in urine flow was not related to the increase in mean arterial blood pressure. During the second stimulation period, the cervical vagi were sectioned bilaterally. This was followed by a reduction in urine flow and a further rise in blood pressure. Subsequent to vagotomy the diuretic response to stellate stimulation was diminished. Table 2 compares the pre- and postvagotomy diuretic and blood pressure response of the fifteen animals in this series. Stellate stimulation produced an increase of 33 mm Hg in mean arterial pressure and an average increase of 1.45 ml/min in urine flow when the cervical vagi were intact. Subsequent to vagotomy stellate stimulation increased mean arterial pressure 30 mm Hg and urine flow 0.68 ml/min. The change in urine flow in response to stellate stimulation following vagotomy was significantly different (P < 0.01) than that observed prior to vagotomy. Vagotomy also diminished the diuretic response in dogs undergoing a mannitol diuresis. Changes in electrolyte concentration, total electrolyte excretion, and inulin clearance, in response to stellate stimulation subsequent to
TABLE 2
Effect of Bilateral Cervical Vagotomy on the Diuretic Response to Left Stellate Ganglion Stimulation

<table>
<thead>
<tr>
<th>Expt. no.</th>
<th>Before vagotomy</th>
<th>After vagotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean arterial pressure</td>
<td>Urine flow</td>
</tr>
<tr>
<td></td>
<td>Cont Stim Cont</td>
<td>Cont Stim Cont</td>
</tr>
<tr>
<td></td>
<td>mm Hg</td>
<td>ml/min</td>
</tr>
<tr>
<td>S-1</td>
<td>125 120</td>
<td>0.10 0.90</td>
</tr>
<tr>
<td>-2</td>
<td>95 145 105</td>
<td>0.15 3.25 0.11</td>
</tr>
<tr>
<td>-3</td>
<td>125 130</td>
<td>0.85 1.80</td>
</tr>
<tr>
<td>-5</td>
<td>103 135 92</td>
<td>0.54 0.72 0.14</td>
</tr>
<tr>
<td>-8</td>
<td>115 122 110</td>
<td>0.28 0.54 0.22</td>
</tr>
<tr>
<td>-10</td>
<td>85 110 95</td>
<td>0.11 1.96 0.40</td>
</tr>
<tr>
<td>-11</td>
<td>77 135 78</td>
<td>0.40 2.18 0.31</td>
</tr>
<tr>
<td>-14</td>
<td>110 133 125</td>
<td>1.28 3.56 0.38</td>
</tr>
<tr>
<td>-18</td>
<td>90 145 93</td>
<td>0.22 1.18 0.24</td>
</tr>
<tr>
<td>-20</td>
<td>128 153 140</td>
<td>0.24 0.54 0.34</td>
</tr>
<tr>
<td>-21</td>
<td>70 125</td>
<td>0.26 1.62</td>
</tr>
<tr>
<td>-22</td>
<td>100 125 98</td>
<td>0.11 1.24 0.16</td>
</tr>
<tr>
<td>-23</td>
<td>85 150 90</td>
<td>0.52 1.68 0.32</td>
</tr>
<tr>
<td>-29</td>
<td>125 145 115</td>
<td>1.90 4.30 1.70</td>
</tr>
<tr>
<td>-30</td>
<td>80 130 80</td>
<td>1.75 4.30 1.20</td>
</tr>
<tr>
<td></td>
<td>80 125 80</td>
<td>1.20 3.75 1.35</td>
</tr>
<tr>
<td>Mean</td>
<td>99 132 100</td>
<td>0.65 2.13 0.57</td>
</tr>
<tr>
<td>± SD</td>
<td>16 12 17</td>
<td>0.78 1.24 0.52</td>
</tr>
</tbody>
</table>

Mannitol diuresis

<table>
<thead>
<tr>
<th>Expt. no.</th>
<th>Before vagotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean arterial pressure</td>
</tr>
<tr>
<td></td>
<td>Cont Stim Cont</td>
</tr>
<tr>
<td></td>
<td>mm Hg</td>
</tr>
<tr>
<td>-34</td>
<td>135 130 130</td>
</tr>
<tr>
<td>-37</td>
<td>98 115 95</td>
</tr>
<tr>
<td>-38</td>
<td>100 115 90</td>
</tr>
<tr>
<td>Mean</td>
<td>111 120 105</td>
</tr>
</tbody>
</table>

* Control.
† Stimulation.
‡ Standard deviation.
vagotomy paralleled the changes in urine flow, i.e., the changes were similarly diminished.

In one experiment the effect of vagotomy at the level of the diaphragm on the diuretic response to stellate stimulation was compared with the effects of cervical vagotomy. This experiment is shown in figure 6. Stellate stimulation was still accompanied by a substantial increase in urine flow when the vagi were sectioned bilaterally a few centimeters above the diaphragm. In contrast, when the cervical vagi were sectioned there was a substantial decrease in the diuretic response to stellate stimulation.

Discussion

The above data suggest that the vagi contain the afferent pathway of a reflex which can modify urine flow and electrolyte excretion in the dog. The receptor component of the reflex appears to be, at least in part, below the cervical region and above the diaphragm. In this region are three well described receptors which might be expected to respond to hemodynamic changes; those of the left atrium, the baroreceptors of the left ventricle and aortic arch, and the aortic chemoreceptors. The atrial receptors do not appear to be those concerned since (a) atrial distension diuresis is associated with increased vagal activity in relation to "v" wave discharge, whereas the diuresis of stellate ganglion stimulation occurs in the presence of a lowered atrial pressure, a smaller "v" wave, and a greater "a" wave, (b) the electrolyte excretion pattern observed during stellate stimulation differs from that seen during atrial distension; also, inulin clearance usually increases during stellate stimulation whereas such a change is reported not to occur during atrial distension, (c) stellate ganglion stimulation diuresis is characterized by a rapid onset, and, with cessation of stimulation, a rapid disappearance whereas atrial distension diuresis usually shows a slow onset and a relatively gradual disappearance.

The baroreceptors respond both to changes in mean arterial pressure and dynamic pressure. Thus, a pulsatile pressure will produce a greater increase in carotid sinus nerve discharge than will a nonpulsatile pressure at a given mean arterial pressure. A characteristic feature of cardiac sympathetic nerve stimulation is the change produced in ventricular and arterial pressures; there is an increase in pulse pressure and in the rate of rise of pressure, both of which would be expected to increase baroreceptor nerve discharge. It appears, therefore, that the baroreceptors of both the carotid sinus and aortic arch are those concerned in the diuresis observed during stellate ganglion stimulation. The participation of the baroreceptors of both these areas would explain why cervical vagotomy diminishes, but does not abolish the diuresis. There is no reason to expect that the changes associated with stellate stimulation modify chemoreceptor discharge.

Wise and Ganong observed that stimulation of areas grouped around the obex in the area postrema of the brain stem of the dog increased creatinine clearance, urine flow, and electrolyte excretion, with little change in mean arterial pressure. As the authors pointed out, afferent fibers from the carotid and aortic baroreceptors enter the medulla in the region of the obex. However, they did not believe that they were eliciting the renal effect by inhibition of sympathetic tone because of the absence of, or minimal, blood pressure effects. The response was blocked by renal denervation. That the efferent portion of the reflex concerned in the stellate diuresis is neural, is suggested by the rapidity of the diuretic response. Since no vasodilator fibers have been shown to innervate the kidney the vasodilation induced by stellate stimulation is presumably the result of sympathetic withdrawal rather than the activation of vasodilator pathways.

In 1959 Atkins and Pearce reported that vagotomy, although not preventing, decreased the extent of the diuresis associated with the administration of intravenous infusions. They concluded that the diuresis was a result of altered tubular function since "variable" changes in glomerular filtration rate were observed. Subsequently, Pearce reported that carotid sinus denervation alone or in combination with vagotomy did not prevent the
diuresis although, under the latter condition, the diuretic response was occasionally absent. It was concluded that the stretch receptors of the carotid sinus are not essential to the diuretic response and do not appear to play a major role. Pearce suggested that the occasional decrease in urine chloride concentration in response to infusion implied a reduced tubular reabsorption of water and a decreased secretion of the antidiuretic hormone. It should be noted, however, that stellate stimulation may also be accompanied by a decrease in electrolyte concentration at a time when there is no reason to expect that a change in circulating ADH had occurred.

On the basis of the decreased diuretic response to infusions subsequent to vagotomy Atkins and Pearce assumed that the effect of vagotomy was to section the afferent nerves leading from the atrial volume receptors, which are believed to influence the secretion of ADH. It will be recalled however, that vagotomy also decreases the diuretic response to stellate stimulation; during stellate ganglion stimulation atrial pressure is decreased, rather than increased as occurs in response to infusion. Thus, the atrial distension receptors do not appear to play an important role in the diuresis observed during stellate stimulation. In fact, according to the atrial receptor hypothesis the lowered atrial pressure should be associated with a reduced urine flow. The reflex pathway, suggested by the data of Dieter and Okada et al., should increase renal nerve activity during stellate stimulation and thus decrease rather than increase urine flow.

![Graph](image-url)

**Figure 7** Experiment illustrating the transient responses of renal blood flow to carotid occlusion. AP = arterial pressure. LT RBP = left renal arterial pressure. LT RBF = left renal blood flow. Mannitol diuresis. Carotid occlusion between two vertical arrows. Left kidney = 50 g. Paper speed 2.5 mm/sec.
It is well-known that in response to large infusions, sympathetic vasoconstrictor discharge is decreased so that a large percentage of the infusion can be accommodated intravascularly without a large increase in blood pressure. This decrease in sympathetic vasoconstrictor tone would, as discussed above, decrease sympathetic discharge to the kidney and yield increases of glomerular filtration rate, urine flow, and electrolyte excretion similar to those which occur during stellate stimulation. Failure to observe changes in glomerular filtration rate at a time when renal electrolyte and water excretion pattern suggests such a change, may be related to the methodology, since small changes which may not be detected by the method can produce significant changes in water and electrolyte excretion. Figure 8 shows that an intravenous infusion may be associated with little change in systemic pressure but substantial decreases in renal resistance.

Failure of both carotid sinus denervation and vagotomy to abolish infusion diuresis might be construed as contrary to the suggestion that infusion diuresis may be mediated, at least in part, by the same mechanism as stellate diuresis. Such a preparation, however, has a high sympathetic tone, and an infusion into such a preparation will probably produce a substantial increase in arterial blood pressure, renal blood flow, glomerular filtration rate, and urine flow.

**Carotid Artery Occlusion**

**Results**

Since the results of the stellate ganglion stimulation experiments indicated that an increase in baroreceptor nerve discharge could increase reflexly, renal water and electrolyte excretion, experiments were undertaken to determine the renal effects of decreasing baroreceptor nerve discharge by occlusion of the carotid arteries. The effects of carotid artery occlusion on inulin and PAH clearance, urine flow, and electrolyte excretion were, however, variable not only from animal to animal but also in the same animal. In some experiments inulin and PAH clearance increased during occlusion while in others a decrease was observed. Also, the two clearances did not always show the same directional changes.
Changes in urine flow during carotid artery occlusion were as variable as changes in the clearances. Urinary excretion of sodium and chloride generally paralleled changes in urine flow. However, the average data from the four experiments of this series showed little change in the renal clearance of inulin and PAH and in the excretion of water and electrolytes. Except for the greater changes in arterial pressure, vagotomy did not appear to modify significantly the responses to carotid artery occlusion. From the inconsistency of these results, it appeared that more than one factor was contributing to the net renal response to carotid artery occlusion. Since carotid artery occlusion is presumably associated with a reflexly induced increase in vasoconstrictor tone as well as an increase in renal arterial pressure, experiments were undertaken to determine the role that each of these factors plays in the response of renal blood flow to carotid artery occlusion. The reader is reminded that in the preparation employed below, the left kidney is perfused from the right common carotid artery so that carotid artery occlusion refers to left common carotid artery occlusion, the right common carotid artery having been previously ligated.

The effect of carotid artery occlusion on left renal blood flow and arterial pressure is shown in figure 7. After a transient decline at the onset of occlusion, renal blood flow rose and stabilized at approximately the control level. Upon release of occlusion renal blood flow initially increased and then declined to the control level. In the twenty-nine experiments done, the control mean arterial pressure was 142 mm Hg and the control left renal blood flow 3.8 ml/min/g. During carotid artery occlusion mean arterial pressure rose to 171 mm Hg and renal blood flow declined to 3.4 ml/min/g. Table 3 shows the transient effects of carotid artery occlusion on left renal blood flow in experiments in which timing and recording speed was such that the appearance times of the flow transients could be determined.

Figure 8 is a record from an experiment in which renal blood flow was maintained constant by a pump. At a constant renal blood flow carotid artery occlusion was accompanied by a substantial increase in renal arterial pres-
## Table 3: Transient Effects of Carotid Occlusion on Left Renal Blood Flow

<table>
<thead>
<tr>
<th>Exp. no.</th>
<th>Carotid occlusion</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RBP* mm Hg</td>
<td>RBF ml/min</td>
</tr>
<tr>
<td>P-20</td>
<td>150/149</td>
<td>189/180</td>
</tr>
<tr>
<td></td>
<td>215/215</td>
<td>218/219</td>
</tr>
<tr>
<td>-21</td>
<td>170/171</td>
<td>197/198</td>
</tr>
<tr>
<td>-29</td>
<td>150/151</td>
<td>210/211</td>
</tr>
<tr>
<td>-22</td>
<td>145/146</td>
<td>185/186</td>
</tr>
<tr>
<td>-23</td>
<td>150/151</td>
<td>175/176</td>
</tr>
<tr>
<td>-17</td>
<td>153/154</td>
<td>158/159</td>
</tr>
<tr>
<td>Mean</td>
<td>154/155</td>
<td>187/188</td>
</tr>
</tbody>
</table>

* Left renal mean blood pressure.  
† Left renal blood flow.  
§ Time between carotid occlusion and initial decline in left renal blood flow.  
|| Time between release of carotid occlusion and initial rise in left renal blood flow.  
|| Standard deviation.
sure. Also, the transient changes in renal arterial pressure were opposite to the changes in renal blood flow observed in those experiments in which renal blood flow was not held constant. (In only a few experiments was renal blood flow pumped at a constant rate since it was noted that perfusing the kidney with a pump produced substantial increases in renal resistance.) At the end of the third carotid artery occlusion in figure 8, 200 ml of donor blood was given intravenously during the time indicated by the two vertical arrows. This was accompanied by a substantial decrease in renal perfusion pressure but only a small increase in systemic arterial blood pressure.

Occasionally, carotid artery occlusion was accompanied by an increase in renal blood flow without observable flow transients. Such a response is shown in figure 9. At A, renal arterial pressure and flow were reduced by increasing renal inflow resistance. At B, the resistance was removed increasing pressure and renal blood flow. At C the resistance was again increased. Between D and E the carotid artery was occluded increasing both renal arterial pressure and blood flow. Between F and G renal arterial pressure was increased to approximately the same extent as occurred during the preceding carotid artery occlusion by decreasing inflow resistance. This resulted in a greater increase in blood flow than that produced during carotid artery occlusion. Between H and I carotid artery occlusion was repeated and between J and K the same pressure change again produced by decreasing inflow resistance. The inflow resistance was removed at L. These data make it clear that some factor other than autoregulation was influencing the renal vascular resistance during carotid occlusion.

That the reflex renal vasoconstriction observed during carotid artery occlusion is produced to a substantial extent via an adrenergic mechanism was shown in three experiments, one of which is illustrated in figure 10. The carotid artery occlusions at A and B were accompanied by a reduction in renal blood flow. At C, 2.5 μg of norepinephrine were injected over a period of about 4 sec into the renal artery inflow line producing a fall in renal blood flow and a slight rise in renal perfusion pressure. Carotid artery occlusion at D

Experiment illustrating the effect of phenoxybenzamine upon the response of renal blood flow to carotid occlusion. AP = systemic arterial pressure. RBF = left renal blood flow. See text for description of figure. Left kidney 30 g. Paper speed 0.25 mm/sec.
was again accompanied by a reduction in renal blood flow. At E, 10 mg of phenoxybenzamine mixed with 3.0 μg norepinephrine were injected into the left renal inflow line over a period of 6 sec. The two drugs were given together to increase the transit time of the phenoxybenzamine through the kidney. Subsequent to the administration of phenoxybenzamine there was little increase in renal blood flow indicating that this kidney had little basal sympathetic vasoconstrictor tone. The two subsequent carotid occlusions (F and G) were accompanied by a slight increase rather than decrease in renal blood flow. At H another 2.5 μg injection of norepinephrine was given at the same rate as the injection at C. This produced a smaller decrease in blood flow than that observed at C prior to the injection of phenoxybenzamine indicating that substantial adrenergic blockade had occurred.

Data presented above could indicate the effect of carotid occlusion on the renal pressure flow relationship only at a given level of pressure and flow. Experiments were therefore undertaken to determine the effect of carotid artery occlusion over a wide range of pressure and flow. A difficulty arose in the early experiments in which a roller pump was employed to modify pressure and flow. It was usually found that to approximate the spontaneous renal blood flow of the animal with the pump a greater pressure was required. Use of the pump was therefore discontinued and renal pressure-flow curves obtained by changing inflow resistance by means of a screw clamp on the left renal artery inflow line. This had the disadvantage that the maximum pressure obtainable was the spontaneous arterial pressure of the animal. However, a wide range of pressure was still available over which the pressure flow relationships could be studied.

Renal pressure-flow relationships were obtained by both stepwise increases and decreases in renal inflow resistance. One such experiment is shown in figure 11. The arrows indicate the direction in which pressure was varied. The renal blood pressure-blood flow plot showed typical curvilinear relationships.
whereas there was a linear relationship between renal arterial pressure and urine flow. Figure 12 shows the effect of carotid artery occlusion on the renal pressure-flow relationship. During carotid occlusion the pressure-flow curve was shifted down to the right although autoregulation was still observed.

**Discussion**

The discrepancies between urine flow and inulin and PAH clearance observed in the present experiments may simply indicate the inability of the clearance methods to detect small changes in blood flow and filtration rate. A second possibility must, however, be considered. Carotid artery occlusion is associated with both an increase in renal sympathetic nerve discharge and an increase in renal arterial pressure. Since the renal medullary circulation appears not to autoregulate and since the medulla appears to have little sympathetic innervation compared to the renal cortex, carotid occlusion would be accompanied by an increase in medullary blood flow even in those circumstances in which total renal blood flow and presumably cortical blood flow remained relatively constant. In such a circumstance an increase in urine flow may take place (fig. 11) as a result of a decrease in renal medullary osmolarity. Even in circumstances in which carotid occlusion decreases renal blood flow and glomerular filtration rate, an increase in urine flow may take place. It would appear, therefore, that urine and electrolyte excretion may show varying responses to carotid occlusion as a result of changes in blood flow distribution independent of a change in total renal blood flow and glomerular filtration rate. The failure of Somlyay and co-workers to observe an increase in free water clearance, and thus evidence for an increase in medullary blood flow during carotid artery occlusion, may have resulted from concomitant decreases in glomerular filtration rate not detected by the method used. The contribution of changes in circulating ADH when carotid artery pressure is reduced must await further clarification.

There is general agreement that carotid artery occlusion is associated with an increase in renal vascular resistance. However, there appears to be no agreement as to the mechanism. Sellwood and Verney suggested that it was a result of an intrinsically developed increase in resistance of the preglomerular vessels and the data of Forster and Maes indicate that the increased resistance may be of a non-nervous origin. It is of interest that the published records of renal blood flow measured using an electromagnetic flowmeter do not show the transient changes usually observed in the present experiments when the carotid artery was occluded and released. In fact, Polosa and Rossi consider the failure to show such changes as an argument against a renal sympathetic influence since they did find a vasodilatation of the hindleg vessels when the carotids were released. However, Heymans observed that when the kidney of one dog was perfused at a constant pressure by a second dog, occlusion of the carotid arteries in the first animal was associated with a reduction in renal blood flow.

While the increase in renal perfusion pressure may play a role in the adjustment of renal blood flow during carotid occlusion, it must be remembered that carotid occlusion is not the usual way in which carotid sinus nerve discharge is decreased in the intact animal. Except in cases of carotid stenosis below the bifurcation of the carotids, low carotid sinus pressure is associated with a decrease in systemic arterial pressure and thus in renal perfusion pressure. This in turn increases sympathetic efferent nerve discharge which tends to maintain pressure at the normal level rather than to increase it. Thus, at the most, compensation would be accompanied by a normal or low blood pressure in the presence of renal vasoconstriction. This, in turn, would be associated with a reduction in renal blood flow, glomerular filtration rate, and water and electrolyte excretion.

**Summary**

Electrical stimulation of the left stellate ganglion of the dog is associated with an increase in urine flow, in electrolyte and total...
solute excretion, and in the renal clearance of inulin. These changes appear rapidly, are well maintained during prolonged stimulation, and stop soon after stimulation has ceased. The hemodynamic responses associated with these changes are an increase in arterial pulse pressure, an increase or no change in mean arterial blood pressure, and a decline in mean left atrial pressure. The diuretic response to stellate ganglion stimulation is diminished, but not abolished, by bilateral cervical vagotomy as are the changes in electrolyte excretion, total solute excretion, and the renal clearance of inulin. However, the hemodynamic responses are not greatly modified by cervical vagotomy. Vagotomy just above the diaphragm does not appear to modify these responses. The effect of vagotomy on the renal responses to stellate stimulation appears to be a result of sectioning baroreceptor afferent nerves which traverse the vagus nerves. The rapidity of the renal response to stellate stimulation, its temporal relation to the hemodynamic changes, and the effect of cervical vagotomy indicate that the diuresis is, to a large degree, secondary to withdrawal of renal sympathetic vasoconstrictor nerve discharge. The similarities between the renal responses to stellate stimulation and to intravenous infusions indicate that infusion diuresis may be mediated, at least in part, by the same mechanism.

When renal blood flow is measured directly in the perfused kidney, carotid occlusion is associated with little change or with a decrease in renal blood flow at a time when renal arterial pressure increases. When renal blood flow is maintained constant in the perfused kidney, carotid artery occlusion is associated with an increase in renal arterial pressure. The intrarenal administration of the adrenergic blocking agent, phenoxybenzamine, can prevent the increase in renal vascular resistance during carotid occlusion indicating that it is due to an adrenergic mechanism. The renal pressure-flow curve is displaced down and to the right during carotid occlusion; autoregulation of renal blood flow is still observed, although at a lower level of blood flow. All these changes indicate that the primary renal response to carotid occlusion is vasoconstriction mediated by the renal sympathetic nerves.

It is well-known that urine flow increases when renal arterial pressure is increased independent of a change in the activity of the renal vasoconstrictor nerves and independent of a change in renal blood flow. Consequently, the rise in arterial pressure associated with carotid occlusion can contribute directly to the response of the kidney to carotid occlusion. The variability of the changes in water and electrolyte excretion by the kidney during carotid occlusion may represent a varying contribution of direct and reflex mechanisms to the total response.

Acknowledgment

The author expresses his appreciation to Dr. S. J. Samoff and Dr. E. M. Renkin for their many constructive criticisms and encouragement during the course of these studies. These experiments were done with the excellent assistance of Mr. Joseph A. Miles.

References

8. PERLMUTT, J. H.: Reflex antidiuresis after oc-


Contribution of Baroreceptors to the Control of Renal Function
JOSEPH P. GILMORE

*Circ Res.* 1964;14:301-317
doi: 10.1161/01.RES.14.4.301

*Circulation Research* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1964 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circres.ahajournals.org/content/14/4/301

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in
*Circulation Research* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the
Editorial Office. Once the online version of the published article for which permission is being requested is
located, click Request Permissions in the middle column of the Web page under Services. Further information
about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation Research* is online at:
http://circres.ahajournals.org/subscriptions/