Effects of Renal and Hepatic Venous Congestion on Renal Function in the Presence of Low and Normal Cardiac Output in Dogs

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SUMMARY  We investigated the effect of acute renal vein and hepatic vein hypertension induced by partial balloon-occlusion of the abdominal inferior vena cava (AIVC-O) and the thoracic inferior vena cava (TIVC-O) on systemic and renal hemodynamics and renal function in 13 dogs anesthetized with pentobarbital. When a renal vein pressure of 13 cm H2O was induced by AIVC-O, cardiac output, stroke volume, central venous pressure, renal blood flow, and renal function (GFR, free water clearance, osmolar clearance, urine output, urinary sodium excretion, fractional sodium excretion) decreased significantly. When systemic hemodynamics were restored to control values by transfusion of autologous blood (mean of 9 ml/kg body weight) while renal vein pressure was kept elevated, renal function also was restored. A hepatic venous pressure of 13 cm H2O then was induced by TIVC-O. The effects on systemic hemodynamics and renal function were very similar to those observed during AIVC-O. When systemic hemodynamics were restored to control values by transfusion (mean of 9 ml/kg), while hepatic venous hypertension was maintained by TIVC-O, renal function also was restored. Despite significant changes in natriuresis and diuresis, intrarenal blood flow distribution, as determined by the radioactive microsphere technique, remained essentially unchanged throughout. We conclude that renal and hepatic congestion induced by partial AIVC-O and TIVC-O do not, per se, alter renal function significantly.


ANTIDIURESIS and antinatriuresis invariably are associated with the use of continuous positive-pressure ventilation in patients with respiratory failure. Renal failure is a common cause of death in the many patients who require continuous positive-pressure ventilation. Although the etiology of impaired renal function is diverse, we have been concerned that the effect of an increase in hepatic venous pressure caused by the institution of positive-pressure ventilation might contribute to the renal dysfunction. Acute hepatic congestion may induce alterations in renal function and intrarenal blood flow distribution (Kilcoyne and Cannon, 1971a; Levy, 1974). Other investigators, however, provided evidence that the retention of sodium and water associated with acute constriction of the thoracic inferior vena cava (TIVC) may be caused by a diminution in cardiac output (Q) or a related decrease in intravascular volume rather than by increased hepatic venous pressure (Schrier et al., 1971). When hepatic congestion is induced by occluding the TIVC, Q decreases, mean arterial pressure falls, and renal vein pressure (RVP) increases (Schrier and Humphreys, 1971). Therefore, it is difficult to differentiate between hepatic congestion, decrease in Q, and increase in RVP as the major stimulus that initiates sodium and water retention during acute TIVC constriction.

Our studies were designed to determine the effects of hepatic congestion induced by acute partial occlusion of the TIVC on renal function and intrarenal hemodynamics. Since an increase in RVP always accompanies the acute occlusion of the TIVC, we first evaluated the effects of partial occlusion of the abdominal inferior vena cava (AIVC) above the renal veins on renal hemodynamics and function. Alterations in systemic hemodynamics were corrected by blood transfusion while RVP was kept constant. Hepatic congestion then was induced by partially occluding the TIVC above the diaphragm. Renal hemodynamics and function were evaluated, first, in the presence of an unconnected Q and, subsequently, when Q was restored to control levels by transfusion. Care was taken to maintain RVP and hepatic vein pressure (HVP) constant during the transfusion. Our results provide information about the relative importance of hepatic venous congestion, renal vein hypertension, and a decrease in Q in inducing the changes in renal function observed during acute partial occlusion of the TIVC.

Methods

In thirteen consecutive experiments we studied mongrel dogs of either sex, weighing 21 to 28 kg. All were deprived of food overnight but had free access...
to water. Anesthesia was induced with pentobarbital (25 mg/kg, iv) and maintained with a continuous infusion of pentobarbital (1.5 mg/kg per hour, iv). All animals breathed room air spontaneously through an endotracheal tube. They were in the supine position and placed on a warming blanket. Body temperature was monitored with an esophageal thermistor.

All dogs received approximately 3.5 ml/kg per hour of Ringer’s lactate solution. Bilateral ureteral catheterization was performed through a suprapubic incision. For direct measurements of total renal blood flow the left renal artery was isolated retroperitoneally through a flank incision. An effort was made to isolate the renal nerves gently without stripping them along with the adventitia. A precalibrated 2.5-, 3.0-, or 3.5-mm electromagnetic flow probe (Statham SP7516) was fitted around the artery and connected to a Statham SP2002 flowmeter whose mean readout was recorded continuously. Catheters were placed into the right atrium and pulmonary artery (Swan-Ganz) via the jugular veins, into the left ventricle via the femoral arteries, into the femoral arteries and advanced to the level of the renal arteries and into the femoral veins and advanced to the level of the renal veins and hepatic veins. Pressures measured at the level of the entry of the renal arteries into the aorta and at the level of the entry of the renal veins and the hepatic veins into the vena cava were considered equal to renal artery, renal vein and hepatic vein pressures, respectively. Pressures were measured with transducers of the Hewlett-Packard 267 and 268 Series and recorded continuously on a multichannel recorder (Sanborn System 7700). Two balloon-tipped catheters were introduced into the inferior vena cava: one was placed with its tip above the renal veins, the other with its tip above the hepatic veins. The correct position of all catheters was verified at the end of each experiment by direct inspection.

Cardiac output was determined in triplicate by the thermodilution technique (Edwards Laboratory, model 9510 cardiac output computer). For this purpose, 10 ml of 5% dextrose in water were injected over 5-10 seconds into the left ventricle. Immediate after aspiration the MS were injected over 5-10 seconds into the left ventricle. With this injection technique we never observed any changes in arterial pressure or pulse rate. MS for a different isotope were injected at the end of any changes in arterial pressure or pulse rate. MS for a different isotope were injected at the end of the various experimental periods.

At the end of each experiment the kidneys were removed, frozen, and the capsule removed by blunt dissection. The kidneys were cut into approximately equal upper and lower polar halves which were then bisected along the sagittal plane to obtain 8 quarter kidneys. Two tissue slices of about 1 cm depth were taken from each quarter kidney. From the most nearly planar surface of each of these slices, a tissue block of approximately 1 cm³ was obtained, and four successive tissue slices of equal thickness were prepared by slicing parallel to the tangent of the capsular surface down to the corticomedullary junction. The cortical slices were numbered sequentially downward from the surface to the medulla, with 1 being the outer and 4 the most inner zone. By this technique we obtained 64 cortical slices from both kidneys, 16 per zone. This procedure served to compensate for variations resulting from inaccurate slicing and anatomic differences.

Each tissue slice was weighed on a Mettler balance and placed in a counting tube. Counting was done in a Packard three-window spectrometer. The counts were corrected for overlaps between the isotopes, tissue weights, and the percent volume of each individual cortex zone, as determined previously (McNay and Abe, 1970). From these data we calculated the percent of total renal blood flow going through each individual zone.

At the beginning of the operative procedure, 500 ml of the dog’s blood was withdrawn while 1,500 ml of lactated Ringer’s solution were being infused simultaneously to obtain blood with similar protein,
electrolyte, and red cell concentrations for the necessary transfusions. This amount of lactated Ringer’s solution for replacement was necessary to avoid hypovolemia and to maintain cardiac filling pressures at pre-hemodilution levels. A few dogs had transient increases in filling pressures which normalized very quickly due to a short-lived increase in urine output. All animals tolerated the isovolemic hemodilution well. The exchange was finished at least 2 hours before the start of the actual experiment. The first experimental period was started only if the urine output did not change by more than 10% during three consecutive 10-minute periods. This was at least 3 hours after induction of anesthesia.

Five 30-minute periods were studied: (1) control period; (2) increase in RVP to approximately 13 cm H2O by partial occlusion of the AIVC above the renal veins; Q was allowed to fall; (3) RVP was kept constant (13 cm H2O), and Q was restored to control values by blood transfusion; (4) increase in HVP to approximately 13 cm H2O by transferring partial occlusion of the inferior vena cava to the TIVC without relieving the renal venous hypertension; Q was allowed to fall; (5) HVP and RVP were kept constant (13 cm H2O) and Q was restored to control levels by blood transfusion. After each experimental intervention, the following period was started only if the urine output did not change by more than 10% over three consecutive 5-minute periods.

At the end of each period, blood was collected for the determinations of sodium, creatinine, hematocrit, oncotic pressure, osmolality, arterial blood gases, and pH. Cardiac outputs were measured and mean aortic pressure, pulmonary capillary wedge pressure (PCWP), central venous pressure (CVP), and temperature were recorded. At this time, MS were injected and urine was collected for volume and clearance determinations. Total peripheral vascular resistance (TPVR), renal vascular resistance (RVR), and renal perfusion pressure (RPP = MAoP minus RVP) were calculated.

All results were analyzed statistically by Friedman’s rank sums test (Hollander and Wolfe, 1973). P values were determined for periods 1 through 3, and for periods 3 through 5.

Results

Occlusion of AIVC above Renal Veins

The AIVC was occluded partially to increase RVP from a mean of approximately 6 cm H2O to a mean of approximately 13 cm H2O. This led to a significant fall in Q from a mean of 3.3 ± 1.3 (standard deviation) 1/min to 2.7 ± 1.2 1/min, stroke volume (19.2 ± 4.9 ml/beat to 15.3 ± 5.3 ml/beat), and CVP (2.6 ± 1.0 cm H2O to 1.8 ± 1.4 cm H2O; Table 1). MAoP did not change, but TPVR increased by almost 30% (3.9 ± 1.1 kilodynes sec/cm2 to 5.1 ± 1.5 kilodynes sec/cm2). Despite a well-maintained RPP, RBF decreased from 166 ± 61 ml/min to 140 ± 58 ml/min and renal vascular resistance increased significantly (81 ± 43 kilodynes sec/cm2 to 100 ± 61 kilodynes sec/cm2). Renal function was affected significantly by the partial occlusion of the AIVC: glomerular filtration rate (GFR) decreased from 65 ± 18 ml/min to 58 ± 18 ml/min, urinary sodium excretion (UN B) from 56 ± 44 μEq/min to 35 ± 29 μEq/min, fractional sodium excretion (FENa) from 0.64 ± 0.54% to 0.40 ± 0.36%, free water clearance (CH2O) from −0.92 ± 0.38 ml/min to −0.76 ± 0.33 ml/min, osmolar clearance (C0m) from 1.31 ± 0.46 ml/min to 1.08 ± 0.40 ml/min, and urine output (U.O.) from 0.41 ± 0.22 ml/min to 0.31 ± 0.11 ml/min (Table 2). Filtration fraction (FF) remained essentially unchanged. Despite significant decreases in RBF and UN B, intrarenal blood flow distribution did not change (Table 3).

Partial Occlusion of AIVC and Restoration of Q

A mean of 9 ml/kg body weight of blood was required to return Q to control levels while RVP was kept elevated at approximately 13 cm H2O. Stroke volume (SV) did not quite return to control levels (17.9 ± 4.6 ml/beat vs. 19.2 ± 4.9 ml/beat), whereas CVP and PCWP slightly exceeded control values; MAoP increased from 154 ± 14 mm Hg to 163 ± 14 mm Hg; TPVR decreased from 5.1 ± 1.5 kilodynes sec/cm2 to 4.5 ± 1.5 kilodynes sec/cm2 but remained 15% above control levels (Table 1). RBF increased from 140 ± 58 ml/min to 151 ± 58 ml/min, but remained 10% below control; RVR remained elevated, and RPP increased slightly, but insignificantly (Table 1). All values, with the exception of MAoP and RVR, are not statistically different from their controls. The correction of the Q resulted in the restoration of all renal function parameters to control levels (Table 2). Again, intrarenal blood flow distribution was unaffected by the induced changes in hemodynamics and renal function (Table 3).

Partial Occlusion of TIVC

The hemodynamic consequences of inducing hepatic congestion by partial occlusion of the TIVC superimposed on partial occlusion of the AIVC are very similar to those observed during the partial occlusion of the AIVC: Q fell from 3.2 ± 1.2 1/min to 2.4 ± 0.8 1/min, SV from 17.9 ± 4.6 ml/beat to 12.9 ± 3.9 ml/beat, and PCWP from 5.9 ± 1.4 to 4.2 ± 1.9 mm Hg. The small decreases in MAoP and CVP did not reach statistical significance (Table 1). TPVR increased significantly from 4.5 ± 1.4 kilodynes sec/cm2 to 5.5 ± 1.6 kilodynes sec/cm2. RVP was kept at approximately 13 cm H2O. The effects on renal hemodynamics are different from those observed during partial occlusion of the AIVC: RBF, RVR, and RPP remained essentially unchanged (Table 1). On the other hand, the effects of partial occlusion of the TIVC on renal function
are very similar: GFR fell from 66 ± 18 ml/min to 54 ± 18 ml/min, $C_{\text{H}_{2}O}$ from −0.93 ± 0.45 ml/min to −0.78 ± 0.25 ml/min, $C_{\text{osm}}$ from 1.45 ± 0.36 ml/min to 1.11 ± 0.30 ml/min, $U_{\text{N},V}$ from 53 ± 32 μEq/min to 27 ± 22 μEq/min, $F_{\text{ENA}}$ from 0.52 ± 0.36% to 0.36 ± 0.29%, and U.O. from 0.52 ± 0.29 ml/min to 0.32 ± 0.14 ml/min (Table 2). Intrarenal blood flow distribution again was unaffected (Table 3).

### Partial Occlusion of TIVC and Restoration of Q
RVP and HVP were maintained at approximately 13 cm H$_2$O. An additional mean of 9 ml/kg body weight of blood was required to return Q to control levels. When this is added to the 9 ml/kg of blood that was required to restore Q after partial occlusion of the AIVC, the total transfusion requirements to maintain Q at control levels during TIVC-occlusion were 18 ml/kg. With the restoration of Q, the other hemodynamic parameters such as SV, $C_{\text{o}_2}$, $C_{\text{Na}}$, PCWP, and TPVR also returned to pre-TIVC-occlusion levels (Table 1). RBF and RPP increased; RVR decreased slightly but insignificantly (Table 1). The restoration of Q to control levels resulted in the correction of all renal function parameters that had been impaired by the partial occlusion of the TIVC (Table 2). Intrarenal blood flow distribution was, again, unaffected (Table 3).

### The Effect of the Experimental Procedure on Various Parameters of General Homeostasis
The effect of the experimental procedure on various parameters of general homeostasis in periods 1 through 5 was as follows (following values are means ± SD): serum sodium concentration (mEq/l) 140 ± 4, 138 ± 4, 139 ± 4, 138 ± 4, 138 ± 4; serum potassium concentration (mEq/l) 3.1 ± 0.4, 3.3 ± 0.4; and hemoglobin concentration (g/dl) 15.3 ± 5.3, 15.3 ± 5.3, 15.3 ± 5.3, 15.3 ± 5.3, 15.3 ± 5.3.

### Table 1: Effect of Experimental Procedure on Systemic and Renal Hemodynamics (n = 13)

<table>
<thead>
<tr>
<th>Effect</th>
<th>1</th>
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<th>4</th>
<th>5</th>
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</thead>
<tbody>
<tr>
<td>Q (liters/min)</td>
<td>3.3 ± 1.3</td>
<td>2.7 ± 1.2*</td>
<td>3.2 ± 1.2</td>
<td>2.4 ± 0.8*</td>
<td>3.2 ± 1.1*</td>
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<tr>
<td>SV (ml/beat)</td>
<td>19.2 ± 4.9</td>
<td>15.3 ± 5.3*</td>
<td>17.9 ± 4.6†</td>
<td>12.9 ± 3.9*</td>
<td>17.5 ± 4.9*</td>
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<tr>
<td>$C_{\text{osm}}$ (ml H$_2$O)</td>
<td>150 ± 14</td>
<td>154 ± 14</td>
<td>163 ± 14</td>
<td>157 ± 19</td>
<td>163 ± 16</td>
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<tr>
<td>CVP (cm H$_2$O)</td>
<td>2.6 ± 1.0</td>
<td>1.8 ± 1.4†</td>
<td>3.0 ± 1.0*</td>
<td>2.3 ± 1.6</td>
<td>3.4 ± 1.9†</td>
</tr>
<tr>
<td>HVP (cm H$_2$O)</td>
<td>4.0 ± 1.4</td>
<td>3.3 ± 1.4†</td>
<td>4.2 ± 1.4†</td>
<td>12.7 ± 0.7†</td>
<td>12.8 ± 0.4</td>
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<tr>
<td>PCWP (mm Hg)</td>
<td>5.3 ± 1.0</td>
<td>4.6 ± 1.4</td>
<td>5.9 ± 1.4†</td>
<td>4.2 ± 1.9*</td>
<td>6.0 ± 1.9*</td>
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<tr>
<td>$TPVR$ (kilodynes • sec • cm$^{-5}$)</td>
<td>3.9 ± 1.1</td>
<td>5.1 ± 1.5*</td>
<td>4.5 ± 1.4†</td>
<td>5.5 ± 1.6†</td>
<td>4.5 ± 1.5†</td>
</tr>
<tr>
<td>RBF (ml/min)</td>
<td>190 ± 61</td>
<td>140 ± 58†</td>
<td>151 ± 56</td>
<td>143 ± 69</td>
<td>162 ± 69</td>
</tr>
<tr>
<td>RVP (ml/min)</td>
<td>146 ± 14</td>
<td>145 ± 14</td>
<td>153 ± 14</td>
<td>148 ± 21</td>
<td>153 ± 16</td>
</tr>
<tr>
<td>$RVR$ (kilodynes • sec • cm$^{-5}$)</td>
<td>5.6 ± 1.4</td>
<td>12.9 ± 0.5*</td>
<td>12.8 ± 0.4</td>
<td>13.2 ± 0.8</td>
<td>13.1 ± 0.9</td>
</tr>
</tbody>
</table>

* = Control period. † = partial occlusion of abdominal inferior vena cava (AIVC-0). ♠ = TIVC-0 plus transfusion. H = partial occlusion of thoracic inferior vena cava (TIVC-0). & = TIVC-0 plus transfusion. Q = cardiac output. SV = stroke volume. $C_{\text{o}_2}$ = mean aortic pressure. CVP = central venous pressure. HVP = hepatic venous pressure. $PCWP$ = capillary wedge pressure. $TPVR$ = total peripheral vascular resistance. RBF = renal blood flow. RVP = renal vein pressure. $RVR$ = renal vascular resistance. All values are means ± SD. Footnote symbols indicate statistical difference ($P < 0.05$) to preceding value.

### Table 2: Effect of Experimental Procedure on Renal Function (n = 13)

<table>
<thead>
<tr>
<th>Effect</th>
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<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR (ml/min)</td>
<td>65 ± 18</td>
<td>58 ± 18†</td>
<td>66 ± 18†</td>
<td>54 ± 18*</td>
<td>64 ± 27†</td>
</tr>
<tr>
<td>$C_{\text{H}_{2}O}$ (ml/min)</td>
<td>−0.97 ± 0.38</td>
<td>−0.76 ± 0.33*</td>
<td>−0.93 ± 0.45*</td>
<td>−0.78 ± 0.25†</td>
<td>−1.04 ± 0.50*</td>
</tr>
<tr>
<td>$C_{\text{osm}}$ (ml/min)</td>
<td>1.31 ± 0.46</td>
<td>1.08 ± 0.40*</td>
<td>1.45 ± 0.36*</td>
<td>1.11 ± 0.30*</td>
<td>1.55 ± 0.54*</td>
</tr>
<tr>
<td>$U_{\text{N},V}$ (μEq/min)</td>
<td>0.41 ± 0.22</td>
<td>0.31 ± 0.11†</td>
<td>0.52 ± 0.29*</td>
<td>0.32 ± 0.14*</td>
<td>0.51 ± 0.22*</td>
</tr>
<tr>
<td>$F_{\text{ENA}}$ (%)</td>
<td>0.64 ± 0.54</td>
<td>0.40 ± 0.36*</td>
<td>0.59 ± 0.36†</td>
<td>0.36 ± 0.29*</td>
<td>0.75 ± 0.54*</td>
</tr>
<tr>
<td>FF (%)</td>
<td>20.5 ± 9.5</td>
<td>21.7 ± 9.5</td>
<td>23.6 ± 9.7</td>
<td>19.9 ± 9.1</td>
<td>20.7 ± 6.3</td>
</tr>
</tbody>
</table>

For explanation of symbols and statistical methods applied, see Table 1. GFR = glomerular filtration rate. $C_{\text{H}_{2}O}$ = free water clearance. $C_{\text{osm}}$ = osmolar clearance. U.O. = urine output. $U_{\text{N},V}$ = urinary sodium excretion. $F_{\text{ENA}}$ = fractional sodium excretion. FF = filtration fraction. All values are means ± SD.

### Table 3: Effect of AIVC-O (n = 6) and TIVC-O (n = 5) followed by Transfusion on Intrarenal Blood Flow Distribution

<table>
<thead>
<tr>
<th>Effect</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone 1 (% of TRBF)</td>
<td>57.3 ± 4.4</td>
<td>55.4 ± 4.7</td>
<td>53.8 ± 4.7</td>
<td>56.0 ± 6.7</td>
<td>57.1 ± 6.3</td>
</tr>
<tr>
<td>Zone 2 (% of TRBF)</td>
<td>27.4 ± 3.2</td>
<td>29.1 ± 3.4</td>
<td>28.0 ± 3.2</td>
<td>28.0 ± 3.6</td>
<td>28.4 ± 3.8</td>
</tr>
<tr>
<td>Zone 3 (% of TRBF)</td>
<td>11.6 ± 2.2</td>
<td>11.8 ± 1.7</td>
<td>13.0 ± 2.0</td>
<td>12.0 ± 2.5</td>
<td>10.9 ± 2.2</td>
</tr>
<tr>
<td>Zone 4 (% of TRBF)</td>
<td>3.7 ± 1.5</td>
<td>3.7 ± 2.0</td>
<td>4.6 ± 1.7</td>
<td>4.0 ± 2.0</td>
<td>3.6 ± 1.8</td>
</tr>
</tbody>
</table>

For explanation of symbols 1-4, see Table 1. TRBF = total renal blood flow. Zone 1 = outer 25% of renal cortex. Zone 2 = next to outer 25% of renal cortex. Zone 3 = next to inner 25% of renal cortex. Zone 4 = innermost 25% of renal cortex. Experimental period 3 is listed twice, because different dogs were used for periods 1 through 3 and period 3 through 5.
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0.4, 3.4 ± 0.4, 3.6 ± 0.4, 3.3 ± 0.4; plasma onocotic pressure (mm Hg) 13.5 ± 1.5, 14.0 ± 1.4, 14.3 ± 1.3, 14.4 ± 1.2, 14.6 ± 1.1; serum osmolality (mOsm/kg) 291 ± 6, 290 ± 5, 290 ± 6, 287 ± 6, 287 ± 5; hematocrit (%) 38 ± 6, 38 ± 6, 39 ± 4, 41 ± 5, 41 ± 5; body temperature (°C) 36.4 ± 0.7, 36.6 ± 0.6, 36.7 ± 0.6, 37.0 ± 0.6, 37.0 ± 0.7; PaO2 (mm Hg) 94 ± 18, 91 ± 13, 95 ± 13, 92 ± 14, 83 ± 14; PaCO2 (mm Hg) 33 ± 7, 32 ± 8, 32 ± 6, 31 ± 6, 31 ± 8. With the exception of the hematocrit and PaO2 values of periods 3 and 5, there were no statistically significant differences (P > 0.05) in any of those parameters between the different experimental periods.

Discussion

A decrease in Q and/or intravascular volume seems to be the main afferent stimulus for the antinatriuretic and antidiuretic responses during acute partial occlusion of the AIVC and the TIVC. As long as Q is maintained, renal or hepatic congestion per se appears to play an insignificant role in inducing the observed changes in renal function. We have shown that changes in renal hemodynamics and function associated with partial occlusion of the AIVC or TIVC occur independently of alterations in intrarenal blood flow distribution. It is true that the induction of renal and hepatic venous hypertension caused significant changes in renal hemodynamics and function. However, both interventions led to decreases in Q and right- and left-sided cardiac filling pressures. When these changes in systemic hemodynamics were corrected by blood transfusions, renal function was restored despite persistent renal and hepatic venous hypertension. Some of our findings are not in agreement with results of previous investigations.

The effects of acute constriction of the AIVC and the TIVC on hemodynamics and renal function have been studied previously (Schrier and Humphreys, 1971). Although the AIVC was occluded to a very similar degree, Q did not fall, mean arterial pressure and TPVR remained unchanged, but RBF, GFR, UNaV decreased significantly in each animal. We observed a mean decrease in Q of approximately 15%. The modest antinatriuretic effect of acute AIVC constriction was contributed to by an elevation in RVP, because when RVP was kept constant, the constriction of the AIVC did not result in any changes of GFR, RBF, or UNaV. Our results suggest that a decrease in Q or intravascular volume is important in inducing the changes in renal function.

It has been suggested that not only a reduction in effective arterial blood volume, but intrarenal congestion per se may cause changes in renal hemodynamics and function (Kilcoyne and Cannon, 1971a). In contrast to constriction of the TIVC, occlusion of the AIVC did not result in changes of intrarenal hemodynamics. However, mean arterial pressure fell on an average at least 20 mm Hg during TIVC occlusion and Q was not measured.

Substantially different effects of constriction of the AIVC and that of the TIVC on systemic hemodynamics have been demonstrated (Schrier and Humphreys, 1971). As mentioned earlier, Q did not fall when only the AIVC was occluded. However, partial obstruction of the TIVC to a degree comparable to that in our experiments, led to a decrease in Q by more than 30%. It is interesting to note that this fall is very similar to the total fall in Q observed in our experiments, when the decrease in Q of approximately 15% following the partial occlusion of the AIVC is added to the 25% decrease in Q that was associated with the partial occlusion of the TIVC. Because of the different effects of acute AIVC and TIVC constriction on systemic hemodynamics, Schrier and Humphreys suggested that this may be an explanation for the different effects of these maneuvers on renal hemodynamics and function. Their findings supported the importance of an elevation in RVP and a diminution in RPP. Despite significant falls in Q and mean arterial pressure, if RVP and RPP were kept constant, GFR and RBF remained unchanged when the TIVC was partially occluded. However, even under those controlled circumstances, a decrease in UNaV persisted, although it was much less pronounced. Subsequently, the same group of investigators demonstrated that acute constriction of the superior vena cava causes a decrease in Q and UNaV similar to that resulting from acute constriction of the TIVC (Schrier et al., 1971). Since this maneuver is not associated with hepatic congestion, the findings indirectly suggested that Q and intravascular volume rather than hepatic congestion per se are responsible for the alteration in renal function.

Hepatic congestion has also been induced by the injection of histamine into the portal circulation of dogs (Levy, 1974) which leads to a selective hepatic venous outflow block (HVOB). The degree of hepatic congestion thus induced may be comparable to that induced in our study. The infusion of histamine resulted in an increase in portal venous pressure from 13.8 to 18.8 cm H2O. Although the absolute pressure appears to be somewhat higher in Levy’s study, the extent of pressure increase was higher in our experiment (increase in HVP from 4.2 to 12.7 cm H2O). The induction of HVOB in Levy’s study resulted in a significant fall in U.O., UNaV and para-aminohippurate clearance (CPAH). Preliminary studies in three animals suggested that Q remains unaffected by the induction of the HVOB. During the actual experiments, mean arterial blood pressure remained unchanged, CVP fell slightly but significantly, and mean hepatic blood flow fell from 788 ml/min to 563 ml/min. Q was not determined. Although these findings suggest a fall in intravascular volume as a cause for the observed changes in renal function, the decrease in UNaV during HVOB, but not the decrease in CPAH persisted even when simultaneous steady state volume expansion with colloid infusions up to 14-16 ml/min caused the
CVP to rise significantly. Neither denervation of the kidneys, continuous angiotensin infusion, or adrenalectomy and α-adrenergic blockade abolished the decrease in UN NaV observed during acute HVOB. Levy concluded from those studies that the congested liver releases a humoral factor that promotes increased tubular transport of sodium.

We were unable to correlate changes in renal hemodynamics and UN NaV with the distribution of intrarenal blood flow. Despite significant decreases in UN NaV in each dog when the AIVC or the TIVC was partially occluded, intrarenal blood flow distribution remained unchanged. Using the inert gas washout method, a significant reduction in blood flow to the superficial renal cortex with no change or increased flow to juxtamedullary regions has been observed when the TIVC was partially occluded (Kilcoyne and Cannon, 1971a). Subhepatic occlusion of the AIVC did not depress cortical blood flow or depressed it only moderately. However, several other investigators found that changes in intrarenal blood flow distribution are not necessary for the development of salt retention during acute caval constriction when the microsphere technique was used for measuring intrarenal blood flow distribution (Slick et al., 1974; Crumb et al., 1977).

The difficulties in reproducing and comparing results obtained by the inert gas washout method (Thorburn et al., 1963) with those obtained by the microsphere technique (McNay and Abe, 1970) have been summarized previously in detail (Katz et al., 1971; Stein et al., 1973). The MS technique assesses glomerular perfusion, whereas the inert gas washout method assesses peritubular, postglomerular hemodynamic status, which does not always reflect the intrarenal distribution of filtration.

A correlation between intrarenal blood flow distribution and renal sodium excretion has been proposed (Barger, 1966). The salt retention of experimental heart failure was attributed to redistribution of intrarenal blood flow from the superficial cortex to the juxtamedullary area, thereby diverting filtration away from the short, relatively salt-losing superficial nephrons. Using the radioactive inert-gas washout method, initial studies of experimentally induced heart failure (Barger et al., 1961), positive end-expiratory pressure ventilation (Hall et al., 1974), and mild renal nerve stimulation (Pomeranz et al., 1968) seemed to support the “redistribution hypothesis.” However, the use of the MS technique, a more direct method for the evaluation of intracortical blood flow distribution, has produced considerable doubts as to the functional significance of redistribution in determining renal sodium excretion (Stein et al., 1973). Our results reemphasize that antinatriuresis can be induced acutely without any changes in the preexisting pattern of intrarenal blood flow distribution.

When Q fell by approximately 15% during partial occlusion of the AIVC, RBF fell in all but one animal. There was no such consistent change in RBF during partial occlusion of the TIVC despite a fall in Q of 25%. RPP was maintained in both instances, but RVP was increased acutely only during AIVC occlusion. It has been suggested (Schrier and Humphreys, 1971) that acute elevation of RVP may contribute to changes in RBF. On the other hand, moderate levels of RVP elevation (10–26 mm Hg) do not appear to change RBF or GFR (Schmid, 1972). Only at RVP of 40–50 mm Hg do RBF and GFR decrease, and renal autoregulation becomes mildly impaired.

Antinatriuresis and antidiuresis associated with the partial occlusion of the inferior vena cava can be explained on the basis of a fall in GFR. This is in agreement with a previous report (Levinsky and Lalone, 1965). There was a dissociation between RBF and GFR during partial occlusion of the TIVC. Despite a significant fall in GFR, RBF remained unchanged. This would suggest that renal blood flow autoregulation was sustained by preferential dilation of the efferent arterioles. We do not know why there was dissociation between RBF and GFR only during the occlusion of the TIVC.

We did not attempt to define the possible efferent pathway(s) that initiate the changes in renal function observed during AIVC and TIVC occlusion. Substantial evidence has accumulated which implicates sympathetic nerve activity in the antinatriuresis of TIVC occlusion (Azer, 1972; Kilcoyne and Cannon, 1971b; Schrier et al., 1971; Slick et al., 1974; Slick et al., 1975). This is supported by our finding of a markedly increased RVR after AIVC occlusion.

What mechanism may be responsible for this increase in renal sympathetic activity? During both interventions, right- and left-sided cardiac filling pressures decreased. It is known that there are sensory endings in the heart whose afferents travel to the central nervous system via the vagi and the spinal sympathetic nerves (Öberg, 1976). Many of the cardiac receptors have been shown to respond to an expansion of the blood volume (Thorén, 1976, 1977). It is conceivable that these receptors sense the fullness of the circulation (Gupta et al., 1966). Experimental evidence suggests that cardiac receptors can exert profound influence on renal sympathetic activity (Clement et al., 1972; Mancia et al., 1973), renal vascular resistance (Mancia et al., 1973; Öberg and Thorén, 1973), renin release (Brennan et al., 1971; Mancia et al., 1975; Zehr et al., 1976; Thames, 1977), and ADH release (Zehr et al., 1969). In rabbits, renal nerve activity has been shown to increase significantly during a 10% hemorrhage and to decrease similarly during a 10% increase in blood volume (Clement et al., 1972). The decrease in intravascular volume in our experiments may have been sensed by cardiac receptors that responded to a decrease in right and left atrial pressures. Stimulation of these receptors may have led to increases in renin and ADH release or a marked increase in renal sympathetic activity. These various effector mechanisms subsequently may have caused the
observed changes in renal function. When cardiac filling pressures had been restored by transfusion, there could have been a decrease in the stimulation of those cardiac receptors, a decrease in the renal sympathetic activity and renin release, and, consequently, restoration of renal function. A very vigorous activation of the sympathetic nervous system, possibly via baroreceptor activity, is further suggested by the dramatic increase in TPVR which maintained MAOP and RFP despite decreases in Q and right- and left-sided cardiac filling pressures. This mechanism also may have led to the constriiction of resistance vessels in the kidney.

If changes in renal function resulting from activity of the sympathetic nervous system are postulated, the neural supply to the kidney must be intact. Despite careful dissection around the renal artery when placing the flow probe, it is difficult to exclude definitely any impairment of the renal innervation. However, since both ureters were catheterized, we always analyzed separately the urine of the right and the left kidney for clearances, electrolytes and volume before calculating the means. The results were always remarkably similar, although the urine from one side came from the kidney around whose artery a flow probe had been placed, whereas that from the other side came from the kidney not subjected to any surgical intervention. We therefore assume that the nerve supply to the kidney was little disturbed, and that at least part of the change in renal function may have been mediated by an increase in renal sympathetic nerve activity.

In summary, we have shown within the experimental set-up used that acute hepatic or renal congestion per se is unlikely to cause significant changes in renal function when Q is maintained. The changes in renal function observed during acute partial occlusion of the AIVC and TIVC seem to be induced primarily by a fall in "effective" intravascular volume, a fall in Q, or consequences thereof. This is suggested by the finding that renal function will return to normal when Q is restored by transfusion despite persistent hepatic and renal congestion. Changes in renal function occurred without changes in RPP. Antinatriuresis was not dependent on changes in intrarenal blood flow distribution.

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Carotid Sinus Baroreceptor Reflex Control of the Circulation in Medial Sclerotic and Renal Hypertensive Rabbits and Its Modification by the Aortic Baroreceptors

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SUMMARY

We studied the reflex control of blood pressure, heart rate, and hindlimb vascular resistance by the carotid sinus baroreceptors in normal (N), experimental renal hypertensive (RH, one kidney renal wrap model), and medial sclerotic (MS) rabbits under urethane anaesthesia using an isolated perfused carotid sinus preparation and auto-perfused hindlimb. The contralateral carotid sinus was denervated. Compared to N rabbits, the blood pressure and hindlimb vascular resistance of RH and MS rabbits were significantly elevated at all carotid sinus pressures 15 weeks after inducing the disease process. The maximum gains of the curves relating carotid sinus pressure to vascular resistance were significantly elevated in the MS and RH rabbits, but those relating carotid sinus pressure to heart rate were significantly reduced. The changes were greatest in the RH group in which the responses also were set to a higher carotid sinus pressure. In the three groups, division of the aortic nerves produced different changes in the sigmoid curves relating carotid sinus pressure to heart rate, blood pressure, and vascular resistance. There was a linear relationship between blood pressure and basal vascular resistance (correlation coefficient 0.88). Circ Res 47: 890–901, 1980

THL activity of the carotid sinus and aortic arch baroreceptors is modified by experimental renal hypertension (McCubbin et al., 1956; Kedzi, 1962; Kreiger and Marsillan, 1966; Aars, 1968; Angell-James, 1973), atherosclerosis (Angell-James, 1974a), and vitamin D-induced medial sclerosis (Angell-James, 1974b). The threshold pressure for the commencement of baroreceptor activity is increased in studies on both whole nerve (McCubbin et al., 1956; Kedzi, 1962; Kreiger and Marsillan, 1966; Aars, 1968) and single fibers in renal hypertensive and atherosclerotic animals (Angell-James 1973, 1974a). The threshold pressures of single baroreceptor fibers in medial sclerotic rabbits is reduced (Angell-James, 1974b), and all studies report a reduced sensitivity of the baroreceptors to changes of blood pressure above their threshold pressure. These changes may be expected to produce a modification of arterial baroreceptors reflex control of the circulation in these conditions. Previous reports (Bouckaert et al., 1937; Goldblatt et al., 1940; Conway, 1955; McCubbin et al., 1956; Alexander and DeCuir, 1966) indicate that baroreceptor reflexes are active in the regulation of acute changes of blood pressure in hypertensive animals. Other evidence has indicated, however, that baroreflex control of the P-P or R-R interval induced by pressor drugs is reduced in hypertension (Bristow et al., 1969; Gribbin et al., 1971; Angell-James and George, 1980) and it is associated with increased pressor responses to infused vasoconstrictor substances (Brown and Maegraith, 1941; Doyle, 1968).

In this study we investigated the carotid sinus baroreceptor reflex control of blood pressure, heart rate, and hindlimb vascular resistance in rabbits with experimental renal hypertension and vitamin D-induced medial sclerosis. In normal animals, carotid sinus baroreceptor reflexes are known to be modified by the concomitant stimulation of aortic baroreceptors. The extent of this modification was
Effects of renal and hepatic venous congestion on renal function in the presence of low and normal cardiac output in dogs.
H J Priebe, J C Heimann and J Hedley-Whyte

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