Circulatory Dynamics in Spontaneous and Nephrogenic Hypertensive Dogs during the Depressor Response to Acute Inflammation

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(with the technical assistance of A. Ellis and F. Williams)

Cardiac output and blood volume are at control levels in unanesthetized hypertensive dogs during the depressor response to acute inflammation. Hence the fall in blood pressure is due to a decreased total peripheral resistance. The accompanying renal hyperemia indicates that decreased resistance in the renal vascular bed accounts for a significant portion of the fall in total peripheral resistance. Drug studies further suggest that acute inflammation operates to lower blood pressure in hypertensive dogs via mechanisms other than complete paralysis of autonomic vasomotor activity.

A N ACUTE inflammatory process with abscess formation induces a sustained reduction of the blood pressure to normotensive levels in both spontaneous and nephrogenic hypertensive dogs.\(^1\) \(^2\) The mechanism of this prolonged depressor response remains obscure.\(^3\) \(^4\) From hemodynamic considerations, the response may be a result of a marked decrease in either cardiac output or peripheral resistance, or both. Since it is not possible to measure changes in the general peripheral resistance except inferentially, we have undertaken to study the cardiac output in hypertensive dogs during an acute inflammatory reaction with abscess formation. Data were obtained in both anesthetized and unanesthetized hypertensive dogs. Renal blood flow was measured concurrently with the cardiac output to aid in evaluating the relative contributions of the renal and extrarenal systemic vascular beds to any observed reduction of total peripheral resistance. Since alterations in blood volume may influence blood pressure, the circulating blood volume and thiocyanate space were also determined.

In the course of this study, some data on the circulatory dynamics of spontaneous hypertension in the dog\(^2\) were obtained.

METHODS

Control cardiac output determinations, utilizing the Fick principle,\(^4\) were done on 14 adult healthy male mongrel dogs in the postabsorptive state. Three of these were nephrogenic hypertensive, three were spontaneous hypertensive and eight were normotensive animals. Determinations were done on unanesthetized and on anesthetized animals. The procedure in the unanesthetized dog was based on a modification of Marshall's method.\(^5\) \(^7\)

For the determination in the anesthetized dog, intravenous sodium pentobarbital (25 mg. per Kg.) was administered until surgical anesthesia (stage 3) was achieved. Oxygen consumption was measured using endotracheal intubation. A number 38 or 40 endotracheal catheter with an inflatable cuff was passed into the trachea under direct laryngoscopic visualization. Nupercaine ointment was used to lubricate the catheter and decrease local irritative reflexes. This was supplemented on occasion by local application of 1% cocaine. Following intubation, the cuff was inflated to obstruct the airway around the catheter, thereby confining respiratory exchange to the lumen of the endotracheal catheter. A clinical spirometer connected to the endotracheal tube recorded oxygen consumption and respiratory rate. Mixed venous blood was obtained by passing a number 8 or 9 Cournand catheter into the right heart under fluoroscopic control. A specially constructed split needle\(^6\) was used to obviate ligation and severance of the external jugular vein on passing the catheter. Arterial blood samples were obtained by direct puncture of the femoral artery. Simultaneous arterial and mixed venous blood samples were drawn during oxygen consumption determina-
tions. The blood samples were drawn into heparinized syringes under oil and transferred immediately to chilled test tubes. Duplicate oxygen determinations by the manometric method of Van Slyke and Neill were initiated shortly after blood was drawn.

Intracardiac and systemic blood pressures were recorded with a Hamilton manometer. The criteria for spontaneous and nephrogenic hypertension in the dog have been described previously. A detailed account of the blood pressure data over many months in all the dogs used in this study was presented in previous reports. Renal clearances were done on the unanesthetized and anesthetized postabsorptive animals according to methods previously described. The renal fraction, or per cent of the cardiac output perfusing the kidney, was calculated from the formula

\[
\frac{\text{renal blood flow (cc./min.)} \times 100}{\text{cardiac output (cc./min.)}}
\]

Blood volume and total available fluid were determined on the trained unanesthetized postabsorptive dogs utilizing Evans Blue Dye (T 1824) and sodium thiocyanate respectively, according to modifications of the method of Gregersen and Stewart.

The inflammatory reaction with abscess formation was produced by subcutaneous injection of 2.5 cc. of turpentine in the left axilla; the criteria for a positive depressor response have been previously described.

Total peripheral resistance (TPR), renal vascular resistance (R_R) and extrarenal systemic resistance (E_R) were calculated from the formulas,

\[
\text{TPR} = \frac{P_m \times 1332}{V_i}
\]

\[
R_R = \frac{P_m \times 1332}{\text{RBF}_i}
\]

\[
E_R = \frac{P_m \times 1332}{V_i - \text{RBF}_i}
\]

or

\[
\frac{1}{R_{RR}} = \frac{1}{\text{TPR}} - \frac{1}{R_R}
\]

where \(P_m\) = mean blood pressure in mm. Hg, \(V_i\) = cardiac output in cc./sec., \(\text{RBF}_i\) = renal blood flow in cc./sec.

Results

Circulatory Dynamics of Spontaneous and Nephrogenic Hypertension

Unanesthetized Dogs. Data on control cardiac output (C.O.) and cardiac index (C.I.) are presented in table 1. Four unanesthetized normotensive dogs had a mean cardiac index index of 3.9 L/min./M²; the range was 3.8 to 4.1. These values are in general agreement with those previously reported by other workers. The unanesthetized spontaneous hypertensive dog had a normal mean cardiac index of 2.9 L/min./M²; the range was 2.7 to 3.1 (table 1). The unanesthetized nephrogenic hypertensive dog also had a normal cardiac index (table 1).

The control renal clearance values and renal fractions of unanesthetized spontaneous hypertensive dogs were in the normal range (table 4). One nephrogenic hypertensive dog (Z36) had clearances at the lower limits of the normal range, the other (Z95) exhibited a definitely reduced renal blood flow and glomerular filtration rate.

All the hypertensive dogs had a normal blood volume and thiocyanate space (table 2). This was true for the spontaneous as well as the nephrogenic hypertensive animals. The mean blood volumes and thiocyanate spaces, respectively, of the normotensive, spontaneous hypertensive and renal hypertensive groups corresponded closely.

Anesthetized dogs. The mean cardiac index for 6 anesthetized normotensive dogs was 3.6 L/min./M²; the range was 2.5 to 4.6 (table 1). These results agree with those previously reported from this and other laboratories. Compared with values recorded in unanesthetized animals, they have a slightly lower mean and a greater range (table 1). Two unanesthetized spontaneous hypertensive dogs had average cardiac index values of 2.8 and 2.9 L/min./M², respectively (table 1). These values are all within the normal range; they agree with data obtained on the unanesthetized spontaneous hypertensive dog. It is therefore apparent that the cardiac output is at normal levels in spontaneous hypertension. In accord with previous findings, we recorded normal cardiac output values in anesthetized nephrogenic hypertensive dogs (table 1).

Renal clearances on 1 spontaneous and 2 nephrogenic anesthetized hypertensive dogs prior to abscess induction yielded results agreeing closely with values in unanesthetized ani-
TABLE 1.—Control Cardiac Output Data

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Weight</th>
<th>S.A.*</th>
<th>No. of determinations</th>
<th>Average A-V Ox Difference</th>
<th>Cardiac Output Range</th>
<th>Average Cardiac Output</th>
<th>Average Cardiac Index†</th>
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</thead>
</table>

Normotensives-Unanesthetized

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<tr>
<th></th>
<th>Ks</th>
<th>M²</th>
<th>Volumes %</th>
<th>L/min.</th>
<th>L/min.</th>
<th>L/min./M²</th>
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<tbody>
<tr>
<td>P1</td>
<td>18.9</td>
<td>.798</td>
<td>2</td>
<td>3.9</td>
<td>3.0-3.4</td>
<td>3.2</td>
</tr>
<tr>
<td>P2</td>
<td>23.4</td>
<td>.915</td>
<td>1</td>
<td>5.9</td>
<td>—</td>
<td>3.6</td>
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<tr>
<td>P4</td>
<td>14.1</td>
<td>.656</td>
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<td>3.9</td>
<td>2.4-2.7</td>
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<tr>
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<td>4.3</td>
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Spontaneous Hypertensives-Unanesthetized

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<tr>
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<td>2</td>
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<td>3.1-3.6</td>
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Nephrogenic Hypertensives-Unanesthetized

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</thead>
<tbody>
<tr>
<td>Z19</td>
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<td>.679</td>
<td>3</td>
<td>4.8</td>
<td>1.8-2.0</td>
<td>1.9</td>
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Normotensives-Anesthetized

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<td>.798</td>
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<td>4.5</td>
<td>1.8-2.1</td>
<td>2.0</td>
</tr>
<tr>
<td>P2</td>
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<td>.915</td>
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<td>2.8</td>
<td>2.6-2.7</td>
<td>2.7</td>
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<td>2.8-2.8</td>
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<tr>
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<td>3.0</td>
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Spontaneous Hypertensives-Anesthetized

<p>| | | | | | | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Z11</td>
<td>18.8</td>
<td>.796</td>
<td>4</td>
<td>4.2</td>
<td>2.0-2.6</td>
<td>2.3</td>
</tr>
<tr>
<td>Z15</td>
<td>14.5</td>
<td>.668</td>
<td>5</td>
<td>3.7</td>
<td>1.7-2.2</td>
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<td>Z39</td>
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<td>2.9</td>
<td>2.1-2.5</td>
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<tr>
<td>Mean</td>
<td>15.3</td>
<td>.691</td>
<td>—</td>
<td>3.6</td>
<td>—</td>
<td>—</td>
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</tbody>
</table>

Nephrogenic Hypertensives-Anesthetized

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</thead>
<tbody>
<tr>
<td>Z36</td>
<td>20.8</td>
<td>.848</td>
<td>6</td>
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<td>1.5-2.0</td>
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<tr>
<td>Z95</td>
<td>22.4</td>
<td>.892</td>
<td>4</td>
<td>5.3</td>
<td>1.8-2.9</td>
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<tr>
<td>Mean</td>
<td>21.6</td>
<td>.870</td>
<td>—</td>
<td>5.5</td>
<td>—</td>
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</tbody>
</table>

* S.A. = Surface area calculated from the formula S.A. = \( \frac{11.2 \times W^{0.467}}{10,000} \) where S.A. = surface area in square meters, and W = weight in grams.

† Average Cardiac Index = Cardiac output corrected to a surface area of 1 square meter, from the surface area data calculated as indicated above.

...mals (table 4). Under anesthesia, dogs Z11 and Z36 had renal fractions within the normal range. Since renal hypertensive dog Z95 had a diminished renal blood flow and normal cardiac output, the renal fraction was reduced (table 4).

Right ventricular, pulmonary arterial and peripheral venous pressures were at normal
levels in both spontaneous and nephrogenic hypertensive dogs.\textsuperscript{20, 21, 22}

\begin{table}[h]
\centering
\caption{Control Blood Volume and Thiocyanate Space Data}
\begin{tabular}{|c|c|c|c|}
\hline
Dog No. & No. of Determinations & Blood Volume & Thiocyanate Space \\
\hline
\hline
Normotensives &  & cc./Kg. & cc./Kg. \\
\hline
1095 & 2 & 92 & 227 \\
Z101 & 4 & 94 & 257 \\
Z102 & 4 & 108 & 255 \\
P1 & 3 & 108 & 339 \\
P2 & 3 & 92 & 297 \\
P3 & 1 & 98 & 331 \\
P4 & 2 & 106 & 332 \\
P5 & 3 & 93 & 302 \\
Z92 & 1 & -- & 309 \\
Z100 & 1 & 63 & 272 \\
\hline
Mean & \multicolumn{3}{c|}{\textbf{——}} & 94 & 294 \\
Lit. & \multicolumn{3}{c|}{\textbf{——}} & 91 & 294 \\
\hline
Spontaneous Hypertensives & & & & \\
\hline
Z11 & 1 & 89 & 276 \\
Z15 & 5 & 82 & 262 \\
Z20 & 2 & 74 & 270 \\
\hline
Mean & \multicolumn{3}{c|}{\textbf{——}} & 82 & 269 \\
\hline
Nephrogenic Hypertensives & & & & \\
\hline
Z36 & 3 & 91 & 272 \\
Z95 & 4 & 83 & 267 \\
Z93 & 3 & 89 & 302 \\
Z14 & 4 & 76 & 291 \\
Z94 & 1 & -- & 278 \\
Z81 & 2 & 66 & 263 \\
Z83 & 2 & 76 & 277 \\
Z33 & 1 & -- & 309 \\
\hline
Mean & \multicolumn{3}{c|}{\textbf{——}} & 80 & 282 \\
\hline
\end{tabular}
\end{table}

* Lit. = Review of data in the literature on blood volume and thiocyanate space of dogs determined with T 1824 and thiocyanate respectively, the figures cited above being an average of all data given by D. D. Bonnycastle.\textsuperscript{14}

\textit{Circulatory Dynamics during the Depressor Response to Acute Inflammation (Abscess)}

\textit{Unanesthetized dogs.} In 2 unanesthetized hypertensive dogs, exhibiting a prolonged depressor response after turpentine injection (Z19, Z20), cardiac output determinations were done on the second, third and fourth day following the turpentine injection. The systolic and diastolic blood pressures fell about 30 mm. Hg to normotensive levels.\textsuperscript{3} During this depressor response, the resting cardiac output obtained in the unanesthetized animal did not vary significantly from those obtained during the control period (table 3 and figure 1). Thus, spontaneous hypertensive dog Z20 had a mean control cardiac index of 2.9 L/min./M\textsuperscript{2}. During the depressor response to injury, the cardiac index values were 2.4, 3.0 and 3.3 L/min./M\textsuperscript{2} on three successive days. Nephrogenic hypertensive dog Z19 had a mean control cardiac index of 2.8 L/min./M\textsuperscript{2}. Following abscess induction, the cardiac index values were 2.6, 2.9 and 2.9 L/min./M\textsuperscript{2} on three successive days (table 3).

In spontaneous hypertensive dog Z20, renal clearances were done on the second day following tissue injury. The blood pressure had fallen from 195/115 to 160/85 mm. Hg. The cardiac output was within the control range (table 3). At this time, renal clearance determinations in the unanesthetized animal revealed a significant renal hyperemia (table 4 and figure 1). The renal fraction increased from 18 per cent before abscess induction to 30 per cent on the second day after turpentine injection. The dog was afebrile at this time.

Renal clearances were done in 3 other unanesthetized hypertensive dogs (Z36, Z95, Z11) during the depressor response to abscess (table 4). In agreement with previous observations,\textsuperscript{4} each exhibited an increased renal blood flow, with little change in glomerular filtration rate and a decreased filtration fraction.

Calculation of vascular resistance in dog Z20 revealed a moderate decrease in total peripheral resistance, a marked fall in renal vascular resistance and no significant change in extrarenal systemic resistance (figure 1).

Blood volume and thiocyanate space were determined during the depressor response to abscess in 4 unanesthetized dogs. None exhibited a change in blood volume (table 5). Three showed no alteration in thiocyanate space; one nephrogenic hypertensive dog had a 22 per
### Table 3—Changes in Cardiac Output of Hypertensive Dogs During the Depressor Response to Tissue Injury

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Type Dog</th>
<th>Wt.*</th>
<th>S.A.†</th>
<th>Days after Injury</th>
<th>B.P.‡</th>
<th>Heart Rate</th>
<th>Respiratory Rate</th>
<th>Oxygen Consumption</th>
<th>A-V O₂ Difference</th>
<th>Cardiac Output</th>
<th>Cardiac Index</th>
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<tr>
<td><strong>Unanesthetized Dogs</strong></td>
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<tr>
<td>Z19</td>
<td>N.H.‡</td>
<td>15.0</td>
<td>.679</td>
<td>Control</td>
<td>210/105</td>
<td>96</td>
<td>32</td>
<td>92</td>
<td>4.8</td>
<td>1.9</td>
<td>2.8</td>
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<td>1.131</td>
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<td>.848</td>
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<td>.796</td>
<td>Control</td>
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<td>139</td>
<td>14</td>
<td>95</td>
<td>4.2</td>
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<td>120/75</td>
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<td>34</td>
<td>110</td>
<td>1.8</td>
<td>6.1</td>
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</table>

*Wt. = weight in kilograms.
†S.A. = surface area, see table 1 for formula used in calculation.
‡B.P. = blood pressure in millimeters of mercury.
§N.H. = nephrogenic hypertensive.
||S.H. = spontaneous hypertensive.

### Table 4—Renal Clearance and Cardiac Output Data in Unanesthetized vs. Anesthetized Hypertensive Dogs during the Depressor Response to Acute Inflammation

<table>
<thead>
<tr>
<th>Dog No. and Type</th>
<th>Days After Injury</th>
<th>B.P.</th>
<th>GFR</th>
<th>RPF</th>
<th>RBF</th>
<th>FF</th>
<th>C.O.</th>
<th>Renal Fraction*</th>
<th>B.P.</th>
<th>GFR</th>
<th>RPF</th>
<th>RBF</th>
<th>FF</th>
<th>C.O.</th>
<th>Renal Fraction*</th>
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<td>133</td>
<td>322</td>
<td>604</td>
<td>34.0</td>
<td>3.3</td>
<td>18</td>
<td>—</td>
<td>195/115</td>
<td>133</td>
<td>322</td>
<td>604</td>
<td>34.0</td>
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<td>118</td>
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<td>2.7</td>
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<td>91</td>
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<td>190/120</td>
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<td>179</td>
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<td>—</td>
<td>—</td>
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<td>190/120</td>
<td>58</td>
<td>179</td>
<td>326</td>
<td>32.4</td>
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<td>—</td>
<td>—</td>
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<td>157</td>
<td>42.9</td>
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<td>3</td>
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<td>Control</td>
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<td>141</td>
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<td>41.1</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>190/115</td>
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<tr>
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<td>337</td>
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<td>—</td>
<td>—</td>
<td>—</td>
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<td>65</td>
<td>192</td>
<td>337</td>
<td>33.9</td>
<td>—</td>
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<tr>
<td>S.</td>
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<td>72</td>
<td>242</td>
<td>331</td>
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<td>—</td>
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<td>42.9</td>
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*Note: B.P. = blood pressure; GFR = glomerular filtration rate; RPF = renal plasma flow; RBF = renal blood flow; FF = filtration fraction; C.O. = cardiac output; S.H. = spontaneous hypertensive; N.H. = nephrogenic hypertensive.
* Renal Fraction RBF/C.O. † Dog was afibrile at this time. ‡ Under anesthesia for 90 minutes at time of B.P. recording. § Under anesthesia for 220 minutes at time of B.P. recording. || Febrile, temperature elevated 1.8 C. above control level. ¶ Under anesthesia for 180 min. at time of B.P. recording.
of normal for this determination in the dog.\textsuperscript{15}

\textbf{Anesthetized dogs.} During the depressor response to tissue injury, cardiac output determinations during anesthesia with sodium pentobarbital were done on dogs Z36, Z95 and Z11. Under these circumstances, the cardiac output was in each case considerably above the control value (table 3 and figure 2). The increases in cardiac output were 245, 67 and 170 per cent respectively.

\begin{table}[h]
\centering
\caption{Changes in Blood Volume and Thiocyanate Space of Hypertensive Dogs during Depressor Response to Acute Inflammation.}
\begin{tabular}{|c|c|c|c|c|}
\hline
Dog No. & Type Dog & Days After Injury & Blood Volume & Thiocyanate Space \\
& & & cc./Kg. & cc./Kg. \\
\hline
Z36 & N.H. \textsuperscript{*} & Control & 88.6 & 302 \\
& & 5 & 86.8 & 320 \\
& & 9 & 93.4 & 304 \\
Z14 & N.H. & Control & 76.3 & 291 \\
& & 5 & 69.0 & 227 \\
Z36 & N.H. & Control & 90.5 & 272 \\
& & 9 & 80.5 & 301 \\
Z15 & S.H. \textsuperscript{†} & Control & 81.8 & 262 \\
& & 2 & 84.3 & — \\
& & 9 & 93.8 & 289 \\
\hline
\end{tabular}
\end{table}

\textsuperscript{*} N.H. = nephrogenic hypertensive.
\textsuperscript{†} S.H. = spontaneous hypertensive.

In these anesthetized dogs, renal clearances were done immediately following the cardiac output determination. Each exhibited a marked depression of renal blood flow, with slight to moderate decrease in glomerular filtration rate and an increased filtration fraction (table 4 and figure 2). This renal ischemia in these anesthetized dogs during the depressor response to tissue injury was in marked contrast to the renal hyperemia these same animals exhibited earlier on the same day in clearances done prior to anesthesia (table 4). Calculation of the renal fraction for these anesthetized dogs revealed a marked depression, in contrast to the considerable rise exhibited by unanesthetized dog Z20 (table 4). Calculation of vascular resistance revealed a marked fall in total peripheral resistance, a considerable rise in renal

![Graph](http://circ.ahajournals.org/)
vascular resistance and a marked decrease in extrarenal systemic resistance (figure 2).

**DISCUSSION**

Spontaneous hypertension in the dog\(^2\) is hemodynamically similar to experimental nephrogenic and human essential hypertension, since all three exhibit normal cardiac output, circulating blood volume, thiocyanate space, venous pressure and pulmonary arterial pressure.\(^{14, \ 18-22}\) The elevated systemic arterial pressure seen in canine spontaneous hypertension must therefore be attributed (as in experimental nephrogenic and human essential hypertension) to an increased peripheral resistance.*

In previous studies\(^1, \ 4\) it was postulated that this increased peripheral resistance is reversible, since these hypertensive dogs respond to acute inflammation with a fall in blood pressure\(^1\) and a renal hyperemia.\(^3\) The present study reveals that during this inflammatory-depressor reaction, no alteration occurs in the cardiac output, blood volume or thiocyanate space of unanesthetized hypertensive dogs. Therefore, abscess induction, in some undetermined way, effects a decrease in total peripheral resistance; this is responsible for the blood pressure fall. This finding verifies the concept that in hypertensive disease the systemic arteriolar hypertonus is reversible.\(^3, \ 18, \ 20, \ 22\)

Renal hyperemia, in the presence of a normal cardiac output and a fall in blood pressure indicates a markedly reduced over-all renal resistance to blood flow.\(^{21, \ 24}\) Since the renal fraction is increased, the decrease in renal vascular resistance is out of proportion to any decrease in resistance in the extrarenal systemic vascular bed. It is not possible to determine precisely whether the decrement in renal vascular resistance alone is adequate to account for the entire depressor response.

Prior to the induction of an acute inflammatory reaction, cardiac output and renal clearance values for animals under anesthesia correspond closely with findings in unanesthetized dogs. Following abscess induction, these values in anesthetized animals are markedly different from those in unanesthetized dogs. The unanesthetized hypertensive dog exhibits a renal hyperemia and unchanged cardiac output dur-

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* We have previously discussed the possible pathogenetic relationship between this increase in peripheral resistance and the somewhat different patterns of renal physiology and morphology in these three types of hypertension.\(^2\)
ing the sustained depressor response to inflammation. The anesthetized animal exhibits a marked renal ischemia and an elevated cardiac output. Thus, neither the induction of an inflammatory process alone, nor the exhibition of pentobarbital anesthesia alone, elicits a cardiac output change. However, the combination of these two factors drastically alters circulatory dynamics; a marked increase in cardiac output ensues. This augmented cardiac output is apparently secondary to a marked acute fall in total peripheral resistance brought about by the combination of the two stressful conditions.\textsuperscript{35, 36} Apparently abscess (chronic effect) and pentobarbital (acute effect) together severely depress peripheral resistance.\textsuperscript{27-29} As resistance to flow decreases, cardiac output increases. This readjustment is accomplished without any recorded deviation in right atrial pressure.\textsuperscript{28} Concurrently the renal blood flow and renal fraction decrease markedly. As the extrarenal systemic resistance falls precipitously, the renal vascular resistance rises sharply. The renal vasoconstriction, together with the increased cardiac output, serves to maintain blood pressure.\textsuperscript{†} These compensatory responses of the circulation are brought about via regulatory mechanisms at present poorly understood. Epinephrine release may be at least partly responsible for the observed cardiorenal dynamic pattern.

Bradley and co-workers\textsuperscript{38} have studied cardiorenal circulatory dynamics in unanesthetized normotensive and hypertensive patients* during an acute afebrile depressor response to pyrogens. Under these somewhat different conditions, the cardiac output and the renal blood flow are both markedly increased. The observed fall in blood pressure is undoubtedly due to a marked reduction in total peripheral resistance, which has a large component in the renal pathway. During the more chronic depressor response to abscess in unanesthetized hypertensive dogs, no such increase in cardiac output occurs. Only when blood pressure homeostasis is placed doubly in jeopardy by the combined insult of inflammation and pentobarbital anesthesia does such an increase in cardiac output result. Under the latter conditions, we observed a decrease in renal blood flow rather than an increase as in Bradley's experiments. It would appear therefore that the mechanisms involved in Bradley's patients and our dogs are not identical.

The mechanism of the reduction in total peripheral resistance during the depressor response to abscess is not apparent. Among the several possibilities previously discussed\textsuperscript{2} and now under investigation in this laboratory, consideration must be given to the role of the nervous system. Barbiturates in anesthetic doses tend to depress the vasomotor apparatus and produce vasodilatation via both a central and peripheral action.\textsuperscript{27-29} These pharmacologic actions of pentobarbital apparently affect a marked additional decrease in total peripheral resistance in hypertensive dogs undergoing a depressor response to inflammation.\textsuperscript{†} This further fall in peripheral resistance superimposed by barbiturates presupposes a considerable degree of residual neurogenic vasomotor activity.

\textsuperscript{*} Stead and co-workers\textsuperscript{27} have postulated that in the presence of an adequate amount of blood, this compensatory response of the cardiac output to an acute fall in peripheral resistance is brought about by active changes in cardiac relaxation and contraction, probably mediated via reflex (not humoral) pathways.

\textsuperscript{†} An alternate possibility must be considered, namely that effective renal blood flow is reduced under these circumstances because of the operation of a renal shunt mechanism.\textsuperscript{29} In this case, the para-aminohippurate clearance would not be a measure of true renal blood flow; our calculation of renal resistance would not be valid. Such a renal shunt would greatly decrease renal resistance, and would thus contribute to the generalized fall in peripheral resistance. The kidney would not serve as a buffer protecting against shock.\textsuperscript{31, 32} In view of recent work, however, it is unlikely that such a shunt mechanism plays a significant role in man or in the dog.

\textsuperscript{‡} It is possible that some other areas of the systemic circuit (e.g., the skin) may also respond with vasoconstriction, but the total effect is a decreased peripheral resistance.

\textsuperscript{*} Normotensive and hypertensive subjects respond in a qualitatively similar manner. We have found that normotensive dogs exhibit a depressor response to abscess qualitatively similar to that of hypertensive animals.\textsuperscript{36}

\textsuperscript{†} The autonomic blocking agent tetrathyamine chloride similarly elicits a further blood pressure fall in such dogs.\textsuperscript{35}
in unanesthetized hypertensive dogs during the depressor response to inflammation; at least some autonomic activity must continue during the sustained depressor response to abscess. Therefore, the inflammatory reaction operates to lower blood pressure without completely paralyzing autonomic control of blood vessels. It remains to be elucidated whether or not the depressor response is due to partial block (depression without paralysis) of neurogenic vasomotor activity.

**Summary**

1. The cardiodynamic pattern of spontaneous hypertension in the dog is essentially similar to that of canine nephrogenic and human essential hypertension. In all three, a dynamic increase in total peripheral resistance prevails which is potentially reversible.

2. The cardiac output and blood volume remain unchanged in unanesthetized spontaneous and nephrogenic hypertensive dogs during the fall in blood pressure which occurs during an acute inflammatory process with abscess formation. The sustained fall in blood pressure is therefore due to a decrease in the total peripheral resistance.

3. During the depressor response to abscess in the unanesthetized hypertensive dog, a renal hyperemia with increased renal fraction occurs which may account for a significant portion of the decrease in total peripheral resistance.

4. The anesthetized (pentobarbital) hypertensive dog responds differently during the depressor response to inflammation. In this animal, an increased cardiac output is seen. Concomitantly, the renal blood flow is markedly reduced. The fact that pentobarbital anesthesia superimposed on abscess results in a marked increase in cardiac output with no further change in blood pressure shows that the total peripheral resistance is further reduced. The kidney does not participate in this reduction in resistance. Instead a marked renal ischemia occurs, perhaps as a compensatory response operating to maintain the total peripheral resistance. This, together with the increased cardiac output, serves to prevent a marked fall in blood pressure.

5. The ability of pentobarbital anesthesia further to reduce total peripheral resistance during the depressor response to inflammation suggests that abscess operates to lower blood pressure in hypertensive dogs without completely paralyzing autonomic vasomotor activity.

**Acknowledgments**

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**References**


Circulatory Dynamics in Spontaneous and Nephrogenic Hypertensive Dogs during the Depressor Response to Acute Inflammation

J. STAMLER, A. P. FISHMAN, L. N. KATZ, S. RODBARD, A. Ellis and F. Williams

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