Responses of Renal Hemodynamics and Function to Acute Volume Expansion in the Conscious Dog

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SUMMARY. The renal vascular and functional responses to acute volume expansion were determined in conscious dogs with all reflexes intact, sinoaortic arterial baroreceptor denervation, arterial baroreceptor denervation plus bilateral stellectomy, and arterial baroreceptor denervation plus bilateral vagotomy. In the intact dogs, when an isotonic saline infusion increased right atrial pressure by 6 mm Hg, arterial pressure increased by 15 ± 3 from 95 ± 3 mm Hg (P < 0.01) and heart rate rose from 87 ± 4 to 135 ± 6 beats/min (P < 0.01), while renal blood flow rose only slightly (4 ± 2%), and calculated renal resistance was not altered significantly. After arterial baroreceptor denervation, volume expansion with saline induced a greater rise in blood flow (16 ± 2%), but did not alter arterial pressure, and calculated resistance fell by 19 ± 3% from 0.72 ± 0.05 mm Hg/ml per min (P < 0.01), while heart rate still increased. After arterial baroreceptor denervation and either bilateral stellectomy or vagotomy, volume expansion reduced renal vascular resistance by similar amounts. When intact animals were volume expanded by 20% of estimated blood volume with isooncotic, isotonic 3% dextran in saline solution, and with renal perfusion pressure held constant, central venous pressure increased by 4.5 ± 0.6 from 1.8 ± 0.4 mm Hg (P < 0.01), renal blood flow increased significantly by 16 ± 5 ml/min (P < 0.05) from 191 ± 30 ml/min, while calculated renal vascular resistance decreased significantly by 0.08 ± 0.02 from 0.62 ± 0.09 mm Hg/ml per min (P < 0.05). Average urine flow rate and sodium excretion 10–60 minutes after expansion increased markedly by 1.85 ± 0.27 ml/min and 9.84 ± 1.13 μEq/min per kg, respectively (P < 0.01). After arterial baroreceptor denervation, volume expansion induced a similar rise in central venous pressure and renal blood flow. The diuretic and natriuretic responses were not attenuated by arterial baroreceptor denervation. After arterial baroreceptor denervation plus bilateral vagotomy, there was a significant and similar rise in renal blood flow, whereas diuretic (urine flow rate rose by only 0.50 ± 0.10 from 0.35 ± 0.08 ml/min) and natriuretic (sodium excretion rose by only 4.83 ± 0.95 from 1.50 ± 0.48 μEq/min per kg) responses were significantly attenuated (P < 0.01). These data indicate that—in the intact conscious dog—vagal afferent mechanisms play an important role in mediating the diuretic and natriuretic responses to acute volume expansion, whereas the changes in renal hemodynamics that occur with volume expansion appear independent of reflex pathways. (Circ Res 54: 185–195, 1984)

IT is currently held that cardiopulmonary low-pressure baroreceptor reflexes play an important role in the control of peripheral hemodynamics in general, and renal vascular resistance in particular. Experiments with partial obstruction of the pulmonary vein-atrial junction or volume expansion to activate low pressure cardiopulmonary reflexes suggest that these maneuvers result in a withdrawal of sympathetic tone, especially to the renal vascular bed (Karim et al., 1972; Clement et al., 1972; Mancia et al., 1973; Mason and Ledsome, 1974; Mancia et al., 1975, 1976; Thoren et al., 1976; Weaver, 1977; Lloyd and Friedman, 1977; Thames and Abboud, 1979). In anesthetized animal preparations, volume loading results in substantial increases in renal blood flow and decreases in renal vascular resistance (Earley and Friedler, 1965; Higgins, 1971; Blantz et al., 1971; Stein et al., 1972; Earley and Schrier, 1973; Thames and Abboud, 1979). These responses have been shown to occur in the absence of high pressure arterial baroreceptor input (Thames and Abboud, 1979; Weaver, 1977) and are abolished by vagal deafferentation (Edis et al., 1970; Clement et al., 1972; Karim et al., 1972; Mason and Ledsome, 1974) and sympathetic (Weaver, 1977).

Numerous studies have also implicated low pressure cardiopulmonary baroreceptors in mediating the enhanced diuresis and natriuresis secondary to acute volume expansion (Gilmore and Weisfeldt, 1965; Gauer and Henry, 1963; Dirks et al., 1980; Goetz et al., 1975; Linden, 1973; Thames, 1978). On the other hand, there are several reports indicating that cardiopulmonary reflexes have little to do with the enhanced response of renal function with volume expansion (Fater et al., 1982; Gilmore et al., 1979; Kaczmarzyk et al., 1981; Knox et al., 1967; McDonald et al., 1970). Since these experiments generally have been conducted in acutely prepared anesthetized animals, it is conceivable that the integrative response to acute volume expansion differs...
in the intact, conscious animal, in which the complicating influences of anesthesia and recent surgical trauma are absent.

The goals of this investigation were to determine (1) the effects of acute volume expansion on renal hemodynamics and renal function, i.e., diuresis and natriuresis, in the intact, conscious dog, (2) the role of changes in renal perfusion pressure, and (3) whether either high pressure arterial baroreceptor reflexes or low pressure cardiopulmonary baroreceptor reflexes with vagal or sympathetic afferents, play a major role in mediating the renal vascular or functional response to acute volume expansion in the conscious dog. To accomplish these goals, we compared the effects of volume expansion with either isotonic saline, or isotonic, isooncotic dextran on measurements of renal blood flow and calculations of renal vascular resistance and determinations of urine flow rate and Na+ excretion in conscious dogs with (1) all their reflexes intact and with renal perfusion pressure held constant or allowed to vary, (2) arterial baroreceptor denervation (ABD), and (3) ABD plus bilateral vagotomy.

Methods

Surgical Procedures

Mongrel dogs of either sex weighing between 20 and 30 kg were anesthetized with sodium pentobarbital (30 mg/kg, iv). Through a midline laparotomy incision in 47 dogs, Doppler ultrasonic or electromagnetic flow transducers (Zepeda Instruments) were placed around either the left or right renal arteries. Care was taken to cause minimal damage to the nerves along the vessels. When electromagnetic flow transducers were implanted, hydraulic cuff occluders were implanted on the renal artery distal to the flow probe for determination of zero blood flow. In five animals through a thoracotomy, catheters were inserted retrogradely into the bladder for concurrent measurement of urine flow rate and Na+ excretion in conscious dogs. The experiments were conducted in 25 dogs by bilateral section of the renal perfusion pressure. Catheters were placed proximal to the flow probe for determination of zero blood flow and placed in an ultrasonic bath for at least 60 minutes before injection. Absence of microsphere aggregation was verified by microscopic examination before injection of microspheres, 0.7 ml of Tween 80 dextran solution (without microspheres) was injected to determine whether the diluent for the microsphere suspension has any adverse effects on measured cardiac or systemic hemodynamics (Millard et al., 1977). One to two million microspheres, suspended in 10% dextran, were injected through the catheter implanted in the left atrium for the determination of blood flow. A reference sample of arterial blood was withdrawn (7.75 ml/min) from a catheter inserted into the abdominal aorta via the femoral artery under local anesthesia on the day of the experiment. Reference sample withdrawal was initiated 10 seconds before the microsphere injection. Total withdrawal time was approximately 90 seconds. At the end of the experiment, the dog was killed, and the kidneys removed. Blocks of the cortex approximately 1 cm^2 were sectioned from one kidney and divided into four equal zones, according to the methods described by Stein et al. (1972). They were weighed and placed individually in a four-channel γ well counter and counted with appropriately selected energy windows. Total radioactivity to the contralateral kidney was also determined. The raw counts in counts/minute (cpm) were corrected for background and crossovers. The percent of blood flow to a particular zone was determined by dividing the total cpm of that zone by the total radioactivity in cpm to the four zones (Stein et al., 1972).

Arterial blood samples were taken before and during volume loading for the determination of arterial pH, Po2, Pco2, and hematocrit. The blood gases were measured with a Radiometer acid-base analyzer (PHM 71 MK2) and blood microsystem (BMS 3MK3) (Radiometer).

Urine was collected by gravity drainage at 10-minute clearance intervals through insertion of Foley catheters (8 Fr. Bordes) into the animal's bladder before every experiment. Urine sodium concentration was determined by a flame photometer (Instrumentation Lab model IL443).
Experimental Protocols

Experiments were conducted in conscious dogs, trained to lie quietly on a table, and fasted for 12–24 hours, but allowed water ad libitum. The experiments in intact dogs were conducted 2 weeks to 2 months after operation. The experiments in dogs with ABD were conducted 10–14 days after ABD. The experiments in dogs with vagotomy were conducted 4–24 hours after vagotomy. Mean and phasic renal blood flow, systemic arterial pressure, and right atrial pressure, as well as heart rate, were monitored continuously during the control state and during volume loading, and for 60 minutes after volume loading. The infusate was prewarmed to body temperature and infused intravenously through a peripheral vein over 5–10 minutes. Isotonic saline (35–40 ml/kg) was infused in 17 intact dogs, 13 dogs with ABD, six dogs with ABD and stellectomy, and 13 dogs with ABD and vagotomy. Three of the dogs with ABD and vagotomy had also undergone stellectomy previously.

A separate group of dogs was used for the experiments on renal function. Isotonic, isooncotic dextran was infused to five intact dogs with renal perfusion pressure uncontrolled. In the remaining experiments, renal perfusion pressure was controlled in seven intact dogs, 10 dogs with ABD, and nine dogs with ABD and vagotomy. Urine samples were collected over 10-minute periods through the Foley catheter. The control period consisted of three 10-minute periods, during which aortic pressure and right atrial or central venous pressure, total renal blood flow, and heart rate were measured continuously and urine was collected. Then the animals were volume-expanded with an isooncotic 3% dextran in isotonic saline solution to 20% of estimated blood volume, i.e., by an average of 18 ml/kg, in 5–8 minutes. The renal hemodynamic and functional responses to acute volume expansion were monitored continuously up to 2 hours after loading.

In two dogs, the vasodilator reserve of the kidney was tested by the intra-arterial injection of 0.5 mg acetylcholine and 3 mg of papavarin. A catheter was advanced through the femoral artery acutely to the abdominal aorta just proximal to the renal artery for injection of these agents.

All data were recorded on a multichannel tape recorder and played back on a direct-writing oscillograph. Mean renal blood flow and mean pressure were obtained with electronic resistance-capacitance filters with 2-second time constants. Renal vascular resistance was calculated as the quotient of mean pressure (arterial—right atrial) and renal blood flow. Means ± SEM were calculated. All responses between groups were compared by analysis of variance (Armitage, 1974), while one response compared to control values was analyzed using Student's t-test for paired comparisons.

Results

Volume Expansion with Isotonic Saline

In intact, conscious dogs, when volume loading with isotonic saline increased mean right atrial pressure by 6 mm Hg, mean arterial pressure rose by 15 ± 3 mm Hg from a control of 95 ± 3 mm Hg (P < 0.01) (Table 1), heart rate rose from 87 ± 4 to 135 ± 6 beats/min (P < 0.01), renal blood flow increased only slightly (+7 ± 3 ml/min from 158 ± 10 ml/min, P < 0.05), and calculated renal vascular resistance did not change significantly from 0.63 ± 0.04 mm Hg/ml per min (Fig. 1; Table 1). These variables

### TABLE 1

<table>
<thead>
<tr>
<th>Effects of Afferent Denervation on the Responses to Volume Expansion with Isotonic Saline, when Right Atrial Pressure was Elevated by 6 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td><strong>Arterial pressure (mm Hg)</strong></td>
</tr>
<tr>
<td>Intact (n = 17)</td>
</tr>
<tr>
<td>ABD (n = 13)</td>
</tr>
<tr>
<td>ABD plus stellectomy (n = 6)</td>
</tr>
<tr>
<td>ABD plus vagotomy (n = 13)</td>
</tr>
<tr>
<td><strong>Heart rate (beats/min)</strong></td>
</tr>
<tr>
<td>Intact (n = 17)</td>
</tr>
<tr>
<td>ABD (n = 13)</td>
</tr>
<tr>
<td>ABD plus stellectomy (n = 6)</td>
</tr>
<tr>
<td>ABD plus vagotomy (n = 13)</td>
</tr>
<tr>
<td><strong>Renal blood flow (ml/min)</strong></td>
</tr>
<tr>
<td>Intact (n = 17)</td>
</tr>
<tr>
<td>ABD (n = 13)</td>
</tr>
<tr>
<td>ABD plus stellectomy (n = 6)</td>
</tr>
<tr>
<td>ABD plus vagotomy (n = 13)</td>
</tr>
<tr>
<td><strong>Renal resistance (mm Hg/ml per min)</strong></td>
</tr>
<tr>
<td>Intact (n = 17)</td>
</tr>
<tr>
<td>ABD (n = 13)</td>
</tr>
<tr>
<td>ABD plus stellectomy (n = 6)</td>
</tr>
<tr>
<td>ABD plus vagotomy (n = 13)</td>
</tr>
</tbody>
</table>

ABD = arterial baroreceptor denervation.  
*Significantly different from control.  †P < 0.05.  ‡P < 0.01.  ††P < 0.001.  †††P < 0.05.  Significantly different from intact, ‡P < 0.05.  Significantly different from ABD alone, ††P < 0.01.
were monitored up to 60 minutes after volume loading, and there was still no evidence of renal vasodilation.

After ABD, when volume loading increased right atrial pressure by 6 mm Hg, mean arterial pressure did not change but heart rate increased from 119 ± 6 to 147 ± 5 beats/min (P < 0.01), and renal blood flow rose by a greater extent than was observed in the intact dogs, 23 ± 4 ml/min from 145 ± 8 ml/min, (P < 0.01). Thus, unlike the intact dogs, after ABD, the renal response to volume expansion was characterized by vasodilation, i.e., renal vascular resistance fell by 0.14 ± 0.03 mm Hg/ml per min from 0.72 ± 0.05 mm Hg/ml per min, (P < 0.01) (Fig. 1; Table 1).

In dogs with ABD and bilateral stellactomy, when volume loading with saline increased right atrial pressure by 6 mm Hg, mean arterial pressure did not change, but heart rate increased from 97 ± 10 to 123 ± 7 beats/min, and renal blood flow rose by 32 ± 9 ml/min from 171 ± 21 ml/min and renal vascular resistance decreased by 0.14 ± 0.03 mm Hg/ml per min from 0.81 ± 0.07 mm Hg/ml per min. Whereas responses of renal blood flow and vascular resistance were not different in these dogs with ABD and vagotomy, from those with ABD alone, it is important to point out that the tachycardia in response to volume loading was abolished in the animals after vagotomy (Table 1). In the three dogs with ABD, stellactomy and vagotomy responses were similar to those in the entire group of dogs with ABD and vagotomy.

Table 2 shows the effect of volume loading on arterial blood gases and pH as well as the hematocrit. Volume loading reduced hematocrit and blood pH slightly in all groups of dogs. This was accompanied by decreases in arterial \text{PO}_2 and \text{PCO}_2 tension.
Effects of Volume Expansion with Isotonic Saline on Hematocrit and Arterial Blood Gases

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Volume expansion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematocrit (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>38.2 ± 2.9</td>
<td>28.2 ± 2.2*</td>
</tr>
<tr>
<td>ABD</td>
<td>41.5 ± 1.6</td>
<td>39.6 ± 2.2*</td>
</tr>
<tr>
<td>ABD and stellectomy</td>
<td>39.6 ± 3.2</td>
<td>32.0 ± 2.9*</td>
</tr>
<tr>
<td>ABD and vagotomy</td>
<td>41.0 ± 2.4</td>
<td>35.0 ± 2.0*</td>
</tr>
<tr>
<td><strong>Arterial pH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>7.38 ± 0.01</td>
<td>7.36 ± 0.01*</td>
</tr>
<tr>
<td>ABD</td>
<td>7.37 ± 0.02</td>
<td>7.34 ± 0.02*</td>
</tr>
<tr>
<td>ABD and stellectomy</td>
<td>7.41 ± 0.02</td>
<td>7.39 ± 0.02</td>
</tr>
<tr>
<td>ABD and vagotomy</td>
<td>7.39 ± 0.01</td>
<td>7.36 ± 0.01*</td>
</tr>
<tr>
<td><strong>Arterial Po2 (mm Hg)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>80.9 ± 2.5</td>
<td>78.7 ± 2.6</td>
</tr>
<tr>
<td>ABD</td>
<td>73.4 ± 2.6</td>
<td>71.3 ± 3.7</td>
</tr>
<tr>
<td>ABD and stellectomy</td>
<td>74.8 ± 3.7</td>
<td>71.4 ± 4.5</td>
</tr>
<tr>
<td>ABD and vagotomy</td>
<td>78.6 ± 3.7</td>
<td>73.6 ± 4.4</td>
</tr>
<tr>
<td><strong>Arterial PcO2 (mm Hg)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>30.0 ± 1.2</td>
<td>25.9 ± 9.8*</td>
</tr>
<tr>
<td>ABD</td>
<td>33.5 ± 2.2</td>
<td>27.6 ± 2.3*</td>
</tr>
<tr>
<td>ABD and stellectomy</td>
<td>32.6 ± 2.1</td>
<td>28.4 ± 3.1</td>
</tr>
<tr>
<td>ABD and vagotomy</td>
<td>32.6 ± 1.9</td>
<td>29.3 ± 1.6</td>
</tr>
</tbody>
</table>

* Significant change from control, P < 0.05.

There were no significant differences in the changes in these variables among the four groups of dogs.

Volume Expansion with Isotonic Isooncotic Dextran

Figure 2 shows a typical experiment where volume loading was accomplished with the infusion of an isotonic isooncotic dextran in saline solution in an intact dog without renal perfusion pressure controlled. The responses in these experiments were similar to the saline series, i.e., arterial, right atrial, and central venous pressures rose with volume expansion, renal blood flow was not altered, and, thus, calculated renal vascular resistance rose (Table 3). To eliminate the complicating influences of the increase in perfusion pressure to the kidneys, the remainder of the experiments with dextran were performed with renal perfusion pressure controlled.

Figures 3–5 illustrate the changes in renal hemodynamics and renal function in response to volume expansion in dogs with renal perfusion pressure controlled. These data were averaged during volume loading and at 10-minute intervals after volume loading. Table 3 illustrates the changes at the end of volume loading and the average changes during the first hour after volume loading, in the intact group of dogs, when mean arterial pressure was

![Graph showing responses to acute volume loading with isotonic isooncotic dextran](http://circres.ahajournals.org)
maintained constant at 109 ± 3 mm Hg (Fig. 4; Table 3), central venous pressure rose by 4.5 ± 0.6 from 1.8 ± 0.4 mm Hg during volume loading, then began to decline and was still significantly elevated from control at 10–60 minutes. This was accompanied by a significant rise (P < 0.05) in renal blood flow of 16 ± 5 from 191 ± 30 ml/min during loading, and renal blood flow remained elevated by an average of 26 ± 9 ml/min over the next hour (Fig. 4; Table 3). Calculated renal vascular resistance decreased significantly by 0.08 ± 0.02 from 0.62 ± 0.09 mm Hg/ml per min during volume loading (P < 0.05) (Fig. 4; Table 3), but was not significantly reduced during the hour after volume loading. These changes were not altered significantly by either ABD or ABD plus bilateral vagotomy. Hematocrit fell with volume loading from 41 ± 1 to 33 ± 2%, as it did with saline loading.

In intact dogs with renal perfusion pressure controlled, the diuresis and natriuresis began almost instantaneously with volume loading, and reached a peak approximately 30–50 minutes later. Urine flow rate increased by 1.85 ± 0.27 from 0.33 ± 0.05 ml/min, while Na+ excretion increased by 9.84 ± 0.58 μEq/min per kg during the 10–60 minute period after volume loading (Table 3). Thus, urine flow rate increased significantly by 0.03 ± 0.02 from 0.62 ± 0.09 mm Hg/ml per min during volume loading (P < 0.05) (Fig. 4; Table 3), but was not significantly reduced during the hour after volume loading. These changes were not altered significantly by either ABD or ABD plus bilateral vagotomy. Hematocrit fell with volume loading from 41 ± 1 to 33 ± 2%, as it did with saline loading.

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3). The values for renal function observed in intact dogs with renal perfusion pressure controlled were not different from those in intact dogs where renal perfusion pressure was allowed to increase.

In dogs with renal perfusion pressure controlled after ABD, the peak increases in urine flow rate and sodium excretion tended to occur earlier (Fig. 4). However, the diuretic and natriuretic responses were not attenuated by ABD. In fact, urine flow rate was significantly greater ($P < 0.05$) during the first 60 minutes after loading, i.e., urine flow rate increased by $2.90 \pm 0.32$ from $0.51 \pm 0.09$ ml/min. The increases in Na$^+$ excretion were not significantly greater in the dogs with ABD when averaged over the first hour after volume loading, but were greater ($P < 0.05$) during the first two 10-minute collection periods (Fig. 4).

Both the diuretic and natriuretic responses to volume loading were significantly diminished in the dogs with ABD plus vagotomy, when compared with either the dogs with ABD alone (Fig. 5) or the intact dogs (Table 3). In the dogs with ABD and vagotomy, urine flow rate rose by only $0.50 \pm 0.10$ from $0.35 \pm 0.08$ ml/min and Na$^+$ excretion rose by only $4.83 \pm 0.95$ from $1.50 \pm 0.48$ μEq/min per kg in the 1-hour period after volume loading (Table 3). The fractions of total water and Na$^+$ load excreted during the first hour were also diminished markedly in the dogs with ABD and vagotomy (Table 4).

Experiments with Radioactive Microspheres

In five intact dogs, the effects of volume expansion with dextran on total and intrarenal distribution of flow were examined, using the radioactive microsphere technique. As shown in Figure 6, although there was a tendency of flow distribution to favor the inner cortex with volume loading, these changes remained small and were not significantly different from control. When total renal blood flow was measured in the contralateral, non-instrumented kidney, renal blood flow did not change either during, or 60 minutes after, volume loading from a control value of $5.47 \pm 1.17$ ml/min per g. Thus, as with the Doppler technique, volume expansion with dextran exerts little effect on total renal blood flow in intact, conscious dogs when arterial pressure is allowed to increase.

Renal Vasodilator Reserve

In two intact dogs, vasodilatory reserve of the renal bed was tested with the intra-arterial injection of acetylcholine and papavarine. Intra-arterial ace-
TABLE 4
Effects of Afferent Denervation on Excretion of H₂O and Na⁺ Load during the First Hour after Volume Loading with Isotonic Isooncotic Dextran

<table>
<thead>
<tr>
<th></th>
<th>H₂O load (ml)</th>
<th>Total H₂O excretion (ml)</th>
<th>% H₂O excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact (n = 7)</td>
<td>452 ± 22</td>
<td>111 ± 16</td>
<td>25 ± 4</td>
</tr>
<tr>
<td>ABD (n = 10)</td>
<td>445 ± 29</td>
<td>174 ± 19†</td>
<td>42 ± 6†</td>
</tr>
<tr>
<td>ABD plus vagotomy (n = 9)</td>
<td>430 ± 29</td>
<td>30 ± 6†</td>
<td>7 ± 2†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Na⁺ load (mEq)</th>
<th>Total Na⁺ excretion (mEq)</th>
<th>% Na⁺ excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact (n = 7)</td>
<td>69.7 ± 3.4</td>
<td>15.0 ± 1.9</td>
<td>21 ± 2</td>
</tr>
<tr>
<td>ABD (n = 10)</td>
<td>68.8 ± 4.4</td>
<td>18.4 ± 1.8</td>
<td>29 ± 3</td>
</tr>
<tr>
<td>ABD plus vagotomy (n = 9)</td>
<td>65.0 ± 4.1</td>
<td>6.9 ± 1.5‡</td>
<td>10 ± 2‡</td>
</tr>
</tbody>
</table>

Significantly different from intact; † P < 0.05, ‡ P < 0.01. Significantly different from ABD alone; * P < 0.05.

dicholine caused a 97% increase in renal blood flow and a 64% decrease in vascular resistance, along with a 39% decrease in arterial pressure. Similarly, papaverine increased renal blood flow by 30%, while vascular resistance and arterial pressure fell by 44% and 21%, respectively.

Discussion

Numerous prior studies conducted in anesthetized animals have indicated that renal hemodynamics can be influenced profoundly by the activation of the low pressure cardiopulmonary baroreflexes. Volume loading with isotonic saline, dextran, or plasma increases renal blood flow substantially, and decreases renal vascular resistance in anesthetized animal preparations (Earley and Friedler, 1965; Higgins, 1971; Earley and Schrier, 1973; Thames and Abboud, 1979). For example, renal blood flow rose in studies of Earley and Friedler (1965), Higgins (1971), and Thames and Abboud (1979) by 63%, 93%, and 54%, respectively, while Stein et al. (1972), and Blantz et al. (1971), using the radioactive microsphere method, found a 26–29% increase in renal blood flow with volume loading. The mechanism of this effect is thought to involve a reflex reduction in renal vascular resistance stimulated by cardiopulmonary low pressure baroreceptor reflex afferent activity either through the parasympathetic or sympathetic arms of the autonomic nervous system (Linden, 1973; Pelletier and Shepherd, 1973; Goetz et al., 1975; Thames, 1978). Activation of this reflex is believed to facilitate the withdrawal of sympathetic efferent activity to the resistance vessels of the kidney, resulting in vasodilation (Edis et al., 1970; Clement et al., 1972; Karim et al., 1972; Mason and Ledsome, 1974; Schad and Seller, 1976). Other evidence that suggests these receptors may reflexly influence blood flow to the kidney includes an increase in the efferent sympathetic nerve activity and renal vasoconstriction in animals with ABD or with arterial baroreceptors at constant pressure during reductions in blood volume, as in hemorrhage (Clement et al., 1972) or vagal block (Oberg and White, 1970; Mancia et al., 1973, 1975; Thames and Abboud, 1979). Weaver (1977) has suggested that cardiopulmonary baroreceptors with sympathetic afferents may also play an important role in the reflex control of renal sympathetic nerve activity in the anesthetized cat. Thus, based on the findings from these previous studies, it might be predicted that acute volume expansion should induce renal vasodilation through a vagal or cardiac sympathetic afferent mechanism.

In contrast to the predicted response, in the present investigation in the conscious dog, little change in renal vascular resistance was observed in response to volume loading with isotonic saline or isotonic isooncotic dextran which induced either low (0–6 mm Hg), moderate (6–9 mm Hg), or intense (9–12 mm Hg), increases in right atrial pressure (Figs. 1 and 2) or during the subsequent 2-hour period (Fig. 2). When renal perfusion pressure was allowed to increase with volume loading, renal vascular resist-

![Figure 6](https://example.com/figure6.png)

**Figure 6.** Effects of acute volume expansion with isotonic, isooncotic dextran solution on renal blood flow (radioactive microspheres) in four different zones of the renal cortex in the conscious dogs. Zones 1–4 represents regions from the outer to the inner cortex. The data were recorded at control, during volume loading, and at 60 minutes after loading.
ance rose and renal blood flow did not change. It is not likely that the lack of response is due to an inadequate activation of the low-pressure baroreceptors, since the volume expansion in the saline series was sufficient to increase right atrial pressure by 12 mm Hg. Clement et al. (1972) found in anesthetized rabbits that an increase in blood volume of as little as 10% can elicit a 41% decrease in renal nerve activity. More recently, Thames and Abboud (1979) found in anesthetized dogs with ABD that acute volume expansion resulting in less than an 8 mm Hg increase in right atrial pressure induced 54% increases in renal blood flow and 40% decreases in vascular resistance which could be reversed by vagotomy.

It was considered conceivable that the role of the cardiopulmonary low-pressure baroreceptors would be more apparent after elimination of the high pressure baroreceptors (Oberg and White, 1970; Mancia et al., 1976, Thames and Abboud, 1979; Karim et al., 1982). After ABD with saline loading, volume expansion did induce renal vasodilation in the conscious dog (Fig. 1). However, this renal vasodilation was not probably due to neural factors in general, and low pressure cardiopulmonary receptors, in particular, for several reasons. First of all, when arterial pressure was controlled, there was no difference in the changes in renal blood flow and vascular resistance between the intact group of dogs and the group of dogs with ABD. Second, neither bilateral stellatec- tomy nor vagotomy altered renal vascular responses to volume loading (Fig. 1). The finding of modest renal vasodilation with volume loading using saline after ABD, but not in intact dogs, is probably related to the fact that arterial pressure did not rise in these dogs. Thus, autoregulatory mechanisms were not opposing the renal vasodilatory response to volume loading. This conclusion is supported by our experiments in the intact animals with dextran infusion and with renal perfusion pressure controlled. When the rise in perfusion pressure to the kidney was prevented, there was modest renal vasodilation during volume loading, even in intact dogs. However, as was observed with the saline infusion experiments, the modest vasodilation could not be attributed to neural factors, i.e., it was not abolished by either ABD or vagotomy (Fig. 3).

It was considered that—although total renal blood flow was not affected to any great extent—the intrarenal distribution of flow may have been altered appreciably with volume expansion, as was observed in previous studies conducted in anesthetized dogs (Blantz et al., 1971; Stein et al., 1972; Bruns et al., 1974). The results from the present investigation, however, do not support this concept, i.e., there was no significant shift in the intrarenal flow distribution during volume loading in the intact, conscious dogs. It is important to note that the radioactive microsphere technique to measure intrarenal blood flow has been criticized on the basis of microsphere skimming (Aukland 1980, 1981; Ofjord and Clausen, 1983). Thus, although there were clear differences between our results in conscious dogs and prior work in anesthetized animals, the question of whether a significant shift in intrarenal blood flow occurs with volume loading remains unanswered. However, the radioactive microsphere technique was also utilized in the present investigation to determine whether implantation of the renal blood flow transducers prevented observation of renal vasodilation due to potential damage to the renal nerves. The experiments using the radioactive microsphere technique demonstrated no change in renal blood flow to either the instrumented or non-instrumented kidney with volume loading, indicating that the implantation of the flow transducers was not responsible for failure to observe significant reflex renal vasodilation with volume loading.

Since the results of the present investigation conducted in conscious dogs differ from those in anesthetized preparations, it was considered that sympathetic nerve traffic would have little effect on the renal vasodilation. Conceivably, in the conscious dog, resting sympathetic tone to the kidney could be minimal and, thus, reduction in sympathetic nerve traffic would have little effect on the renal circulation. It should be noted, however, that a reflex withdrawal of sympathetic efferent activity to the kidney was observed in the conscious cat in response to volume expansion (Schad and Seller, 1976). Whether this was sufficient to cause changes in renal hemodynamics is not known, since blood flow to the kidney was not measured in that study. However, recent experiments in our laboratory in which blood flow and renal nerve activity were measured indicate that volume loading reduces renal nerve activity dramatically in the conscious dog without significant vasodilation (Morita et al., 1983). Gross and Kirchheim (1980) found that bilateral carotid occlusion elicited little change in renal blood flow, but did increase renal nerve activity. Thus, it appears that in the conscious animal, alterations in sympathetic efferent activity may not always result in concomitant changes in renal hemodynamics, but may have an important effect on renal excretory function.

The results of the present experiments suggest that neither the high pressure arterial baroreceptor nor low pressure cardiopulmonary baroreflexes with vagal or sympathetic afferents are responsible for the modest renal vasodilation observed with volume expansion in dogs with ABD. Bishop and Peterson (1976), although not examining the renal bed, found that neural mechanisms did not mediate changes in total peripheral resistance with volume loading. This concept is further supported by a study of Barron and Bishop (1982) in the conscious dog. They observed that activation of vagal afferents by stimulating the Bezold-Jarisch reflex, elicited significant vasodilation in the limbs, but not the renal bed.
The modest renal vasodilation observed with volume expansion in this investigation could be explained by decreases in hematocrit and blood viscosity, which, by itself, would decrease renal vascular resistance at any given arterial pressure. It is important to note that hematocrit fell during volume loading in these experiments. The data from a study by Fan et al. (1980) supports this concept and suggests that a majority of the decreases in calculated resistance in the kidney can be attributed to a fall in viscosity secondary to hemodilution during volume loading. They have observed that, with a fall of hematocrit from 45 to 22%, there was a fall in calculated renal vascular resistance of 11%.

In the present experiments with isotonic, isoncotic dextran infusion, measurements of renal function were also assessed. The peak diuresis and natriuresis occurred 30–50 minutes after volume loading. Neither the diuresis nor the natriuresis was affected significantly by regulating renal perfusion pressure in the intact dogs (Table 3). For all other experiments, perfusion pressure was regulated.

The arterial baroreceptors were not responsible for either the diuresis or natriuresis secondary to volume loading, since these responses occurred earlier and were actually greater in dogs with chronic arterial baroreceptor denervation. This is in contrast to what was observed in anesthetized dogs by Gilmore and Weisfeldt (1965). In their study, although the increase in Na⁺ excretion was not altered, the diuretic response to volume expansion was attenuated by ABD. In contrast, Gross et al. (1981) found that bilateral carotid occlusion in conscious dogs did not have any significant effect on renal function, independent of changes in renal perfusion pressure.

Henry and Gauer (Henry et al., 1959; Gauer and Henry, 1963) advanced the concept that the low pressure cardiopulmonary baroreflexes with vagal afferents can have profound influence on renal function. The mechanism for this reflex appears to be mechanoreceptors situated in the cardiopulmonary area activating the vagal and/or sympathetic afferent fibers to control renal function. Although increases in renal excretory function have been repeatedly demonstrated by mechanical stretch of the atria (Lydtin and Hamilton, 1964; Linden, 1973; Goetz et al., 1975; Fisher et al., 1982; Schultz et al., 1982), distention of the left atrium by balloon inflation (Ledsome et al., 1961; Kappagoda et al., 1974; Zehr et al., 1976), and volume expansion (Gilmore and Weisfeldt, 1965; Fater et al., 1982), it remains controversial whether the responses of renal function are mediated by vagal afferents. For example, Gilmore and Weisfeldt (1965) failed to demonstrate any difference in the natriuretic response of the kidney to acute volume expansion before and after bilateral vagotomy in the anesthetized dog. The studies by Fater et al. (1982) and Schultz et al. (1982) in conscious dogs suggested that the enhanced renal function elicited by inflation of a balloon in the left atrium, but not that induced by volume loading, could be abolished by cardiac denervation. However, it should be noted that Fater et al. (1982) left the arterial baroreceptors intact. Kaczmarczyk et al. (1981) found that left atrial distention elicited changes in renal function from stimulation of atrial receptors, but that similar effects could be observed, in the absence of cardiac nerves. Gilmore and coworkers (Gilmore and Zucker, 1978a, 1978b; Gilmore et al., 1979), concluded that vagal pathways do not play an important role in the control of renal function in the nonhuman primate. In the present investigation, carried out in conscious dogs responses of urine flow and Na⁺ excretion attenuated significantly by bilateral vagotomy. The fact that after vagal deafferentation, the diuretic as well as the natriuretic responses in these conscious dogs to volume expansion were attenuated indicates that both the control of water and Na⁺ excretion is likely to be mediated by the vagal afferents.

In summary, the data from the present investigation do not support the concept that activation of the cardiopulmonary low pressure baroreceptor reflexes with acute volume expansion induces significant neurally mediated renal vasodilation in the conscious animal. These studies also do not support the position that the vagal or sympathetic afferents play a significant role in the renal vascular response to acute volume expansion in the conscious dog. Moreover, our data do not support the concept that the high pressure baroreceptor reflex plays an important role in the regulation of renal function in the intact conscious dog. However, the diuretic and natriuretic responses to acute volume loading appear to involve the vagal afferents. Whether or not these reflexes play a significant role in the chronic regulation of blood volume remains to be determined.

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