Renal Hemodynamics and Function with Continuous Positive-pressure Ventilation in Dogs

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Renal blood flow obtained by a square-wave electromagnetic flowmeter and intrarenal distribution of blood flow assessed by $^{85}$Kr washout-curve analysis were measured in ten dogs lightly anesthetized with pentobarbital. Creatinine clearance, sodium excretion, and fractional sodium reabsorption were measured in ten dogs, including four of the dogs studied for renal hemodynamics. Comparisons were made between the effects of intermittent positive-pressure ventilation (IPPV) and continuous positive-pressure ventilation (CPPV) with 10 cm H$_2$O positive end-expiratory pressure (PEEP). A 29 per cent decrease in cardiac index caused by CPPV was associated with a 9 mm Hg decrease in mean arterial pressure (P < 0.02) and only a 7 per cent decrease in total renal blood flow (N.S.). With CPPV, fractional perfusion of outer cortex decreased, while perfusion of inner cortex and outer medullary tissue increased, urinary output decreased 40 per cent (P < 0.01), creatinine clearance declined 20 per cent (P < 0.001), sodium excretion decreased 63 per cent (P < 0.005), and fractional reabsorption of sodium increased (P < 0.005). All changes were reversible. The response to the decreases in cardiac index and intrathoracic blood volume during CPPV results in redistribution of intrarenal blood flow and a marked decrease in renal excretion of sodium and water, while total renal blood flow remains essentially unchanged. (Key words: Kidney, mechanical ventilation; Ventilation, mechanical, kidney.)

FLUID RETENTION and decreased urinary output are frequently encountered in patients being supported with continuous positive-pressure ventilation (CPPV). The mechanisms involved are at least twofold, as postulated in 1947 by Drury, Henry and Goodman: release of antidiuretic hormone (ADH) and changes in renal perfusion.¹ Most investigations have focused on the role of central osmoreceptors, intrathoracic volume receptors, and ADH release in causing antidiuresis during CPPV.²⁻⁴ Baratz and Ingraham⁵ found an increase in plasma ADH in dogs ventilated with positive end-expiratory pressure (PEEP), and later, Baratz, Philbin, and Patterson showed the increase to be independent of the left atrial volume receptors.⁶

The contribution of altered renal hemodynamics to the antidiuresis of PEEP remains controversial. Murdaugh, Sieker, and Manfredi⁷ measured decreased insulin clearance, p-aminohippurate (PAH) clearance, and urinary flow in healthy human volunteers breathing with PEEP. They concluded that an increased ADH plasma level was the primary mechanism causing the antidiuresis. Baratz and Ingraham⁸ noted decreases in glomerular filtration rate (GFR), effective renal plasma flow, and urinary flow with a concurrent increase in plasma ADH during CPPV and concluded that both depressed renal hemodynamics and increased plasma ADH were instrumental in the antidiuresis of PEEP. Recent studies have demonstrated significant decreases in sodium excretion in both dog and man ventilated with PEEP.⁹⁻¹³ Changes in sodium excretion are intimately related to renal hemodynamics and the neurohormonal regulation of intrarenal blood flow.¹⁰⁻¹³

In an effort to clarify the role of altered renal hemodynamics in the sodium and water retention associated with PEEP, we have

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studied the effects of CPPV on the intrarenal distribution of blood flow using the $^{85}$Kr-washout technique of Thornburn et al.\textsuperscript{14}

Methods

Sixteen fasted mongrel dogs (14–22 kg) were lightly anesthetized with sodium pentobarbital (28–30 mg/kg, iv, initially and 60–90 mg, iv, each hour thereafter). A cuffed tracheal tube was inserted and succinylcholine (100 mg, im) was administered intermittently to facilitate controlled ventilation with an Emerson postoperative constant-volume sinusoid-flow ventilator. Tidal volume was 20 ml/kg body weight; rate was 20 breaths/min with an inspiratory:expiratory ratio of 1:2. To minimize compression volume changes as the ventilatory pattern was alternated between IPPV and CPPV, a Berry nonrebreathing valve was placed between the ventilator and the tracheal tube.\textsuperscript{15} When CPPV was used, positive end-expiratory pressure (PEEP) of 10 cm H$_2$O was obtained by partial occlusion of the expiratory port of the Berry valve. Tidal volumes were measured with an in-line Wright respirometer at the proximal end of the tracheal tube. The inspired gas consisted of 100 per cent O$_2$ with CO$_2$ added to maintain normocapnia. All dogs were supine on a K-thermia blanket (model R.K. 101, Gormann- Rupp Industries), and body temperature was monitored by an esophageal thermistor (Yellow Springs Co.).

All dogs received Ringer's lactate solution, 10 ml/kg/hr, during the surgical procedure and during an ensuing 2-hour recovery period; thereafter, they received 6 ml/kg/hr. Intra-aortic and suprarenal inferior vena caval catheters were positioned via femoral cutdowns. Bilateral ureteral catheters were inserted through lower abdominal midline incisions, which were immediately closed. The first ten dogs were studied for intrarenal distribution of blood flow and total renal perfusion. The right renal artery was gently isolated with its nerve plexus intact through an incision in the flank. A precalibrated 2.5-mm, 3.0-mm, or 3.5-mm extravascular square-wave electromagnetic flow probe (Statham SP7516) was snugly fitted around the artery and connected to a Statham SP2002 flowmeter (with incorporated non-occlusive zero) whose mean readout was recorded continuously. An intra-arterial 21-gauge scalp vein needle was carefully positioned in the direction of flow proximal to the flow probe. The right kidney was returned to its original position and the incision closed.

Following operation and the 2-hour recovery period, the dogs were ventilated for five one-hour periods alternating between IPPV and CPPV (IPPV$_1$-CPPV$_1$-IPPV$_2$-CPPV$_2$-IPPV$_3$). During the last 10 minutes of each period, arterial blood gases, pH, hematocrit, cardiac output, and urinary output were measured. Continuous recordings of mean aortic pressure, mean suprarenal inferior vena cava pressure, and airway pressure were obtained. In the ten dogs studied for renal hemodynamics a 10-minute $^{85}$Kr-washout curve was measured at the end of each period of ventilation and mean renal blood flow and renal arterial pressure continuously recorded. Hourly determinations of creatinine clearance, sodium excretion, and fractional sodium reabsorption were made in ten dogs, including four dogs simultaneously studied for renal hemodynamics. Serum sodium and creatinine concentrations were measured 30 minutes after the beginning of each period. At the end of the experiment the right kidney was excised, stripped of all fat, and weighed.

Serum and urinary creatinine levels were measured by a Technicon N-11B AutoAnalyzer using the Jaffe reaction. Serum and urinary sodium concentrations were determined by flame photometry. Arterial blood gas tensions and pH were determined at 37 C with a Radiometer microelectrode unit (type E5021). Cardiac output was measured by dye-dilution technique with cardigreen and a Gilson densitometer (model DTL); curves were analyzed by standard planimetric techniques and cardiac outputs calculated. Mean aortic pressure (Hewlett-Packard H-P 267AC transducer), mean renal arterial pressure (H-P 268B transducer), and mean suprarenal inferior vena cava pressure (H-P 268B transducer) were continuously recorded via H-P 1100C preamplifiers in a H-P 7718 oscillographic recording system. Total renal vascular resistance ($R_R$) was calculated by the equation

\[ R_R = (\bar{P}_{RA} - \bar{P}_{IVC})/\bar{Q}_{RAG} \]  

(1)
where $P_{BA}$ is the mean pressure in the renal artery, $P_{VC}$ is the mean pressure in the suprarenal inferior vena cava, and $Q_{RAG}$ is total renal blood flow per 100 g renal tissue. Airway pressure (H-P 268B transducer) was obtained through a blunt needle at right angles to the proximal end of the orotracheal tube and recorded via a H-P 2700C high-gain amplifier in the H-P recording system.

**Measurement of Intrarenal Blood Flow Distribution**

Intrarenal perfusion was studied using the inert-gas-washout technique developed by Thornburn et al. Ten minutes before the end of each ventilatory pattern 2 mCi of $^{85}$Kr in 0.3 ml physiologic saline solution were injected into the renal artery, immediately followed by 1.0 ml heparinized arterial blood at 37 C over 3 seconds. This technique eliminated changes in renal arterial blood flow associated with intra-arterial injections. The rate of disappearance of $^{85}$Kr was monitored with a 1.5-inch NaI scintillation crystal in a cylindrical collimator placed over the closed incision in the flank. The output from the crystal was fed into a digital ratemeter and recorded by teletypewriter in both printed and paper-tape forms. The original technique as described by Thornburn et al. employed a 60-minute counting period. They subsequently found that accurate measurements of component I and component II could be obtained from disappearance curves measured during the first 6 minutes of washout. Others have used counting periods from 5 to 20 minutes. In the present experiments a 10-minute disappearance curve was recorded. The counts were integrated over 2-second intervals during the first 2 minutes and over 6-second intervals for the last 8 minutes.

**Methods of Analysis of $^{85}$Kr Washout Curves**

The multiexponential disappearance of $^{85}$Kr activity recorded over the kidney was compartmentally analyzed by the peeling method. Only one exponential function (compartment III) could be distinguished during the last 6 minutes of the 10-minute disappearance curve. The zero time intercept ($a_0$) and clearance constant ($k_3$) for the exponential function describing the washout of $^{85}$Kr in compartment III were derived from the analysis of the last 6 minutes (60 points) of the 10-minute curve, using a least-squares fitting program. This exponential function was then subtracted from the first 4 minutes of the disappearance curve. The resulting curve was resolved into two exponential functions (compartments I and II) whose clearance constants ($k_1$, $k_2$) and zero time intercepts ($a_1$, $a_2$) were also calculated by the least-squares method. To minimize subjective bias in the analysis of the curves, care was taken to select a constant number of data points measured during the same time interval for all five curves in each dog. Adequacy of fit was checked by superimposing the computer-generated curve over the original data.

Kety, Thornburn et al., and Lådefoged et al. have detailed the equations and theory supporting the analysis of intrarenal blood flow as a multiexponential function. The perfusion rate of the $i$th compartment ($F_i$) in ml/min/100 g tissue is calculated by the equation

$$F_i = k_i \times \frac{\lambda}{\rho} \times 100$$

(2)

where $\rho$ is the specific gravity of the tissue (approximately 1 g/cc for kidney) and $\lambda$ is the tissue: blood partition coefficient of Kr, which is 0.96. The percentage of total renal blood perfusing the $i$th compartment ($A_i$) is calculated by the equation

$$A_i = \frac{a_i}{\sum a_i} \times 100$$

(3)

and relative volume of kidney perfused by the $i$th compartment ($V_i$) is calculated from the equation

$$V_i = \frac{a_i/k_i}{\sum \frac{a_i}{k_i}} \times 100$$

(4)

Autoradiographic studies have repeatedly shown that compartment I represents perfusion of the outer two thirds of the renal cortex and compartment II represents perfusion of the inner portions of the cortex and the
TABLE 1. Effects of CPPV on Hemodynamics in Ten Dogs (Means ± SE)

<table>
<thead>
<tr>
<th></th>
<th>Cardiac Index (CI) (l/min/m²)</th>
<th>Urinary Output (ml/min)</th>
<th>Renal Arterial Blood Flow (Qra) (ml/min)</th>
<th>Qra/Qr* (Per Cent)</th>
<th>Psa (mm Hg)</th>
<th>Psc (cm H₂O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPPV</td>
<td>3.50 ± 0.30</td>
<td>0.53 ± 0.07</td>
<td>203 ± 17</td>
<td>7.8 ± 0.6</td>
<td>156 ± 4</td>
<td>6.9 ± 0.5</td>
</tr>
<tr>
<td>CPPV</td>
<td>2.49 ± 0.18</td>
<td>0.30 ± 0.05</td>
<td>190 ± 18</td>
<td>10.0 ± 0.8</td>
<td>147 ± 4</td>
<td>13.0 ± 0.7</td>
</tr>
<tr>
<td>P‡</td>
<td>&lt;0.002</td>
<td>&lt;0.01</td>
<td>N.S.</td>
<td>&lt;0.001</td>
<td>&lt;0.02</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Qra/Qr = per cent cardiac output delivered to right kidney.
† Psa = mean renal arterial pressure.
‡ Psc = mean suprarenal inferior vena caval pressure.
§ P values from paired Student’s t test.

capillary-rich areas of outer medullary tissue. Compartment III, derived in this experiment, includes both the third and fourth compartments described by Thornburn et al., which represent perfusion of inner medullary tissue and perirenal fat, respectively. Since perfusion of perirenal fat and perfusion of inner medullary tissue were not differentiated in this experiment and since these two areas have been shown to contain little radioactivity in the early portion of the disappearance curve, the percentage of renal volume occupied by compartments I and II was calculated according to the method of Carrière et al. Total renal blood flow, obtained by analysis of ⁸¹Kr-washout curves (F), was estimated as the weighted harmonic mean of compartments I and II by the equation

\[
\bar{F} = \sum_{i=1}^{2} V_i F_i
\]

STATISTICAL ANALYSIS

All analyses were performed on a PDP-10 computer. To assess the effects of the application of 10 cm H₂O PEEP on the various physiologic variables examined in these experiments, the mean of the three measurements of a given variable for each dog during IPPV was paired with the mean of the two measurements during CPPV. These paired means were compared statistically with Student’s paired t test.

The reversibility of changes was assessed by Student’s paired t test, comparing values measured during each experimental period with those obtained during the preceding hourly period. Statistical correlation between variables was assessed by within-group analysis.

Results

RENAL HEMODYNAMICS DURING CPPV

The application of 10 cm H₂O PEEP produced a 29 per cent reduction in cardiac index (CI) and a 9 mm Hg fall in mean renal arterial pressure (table 1). Mean renal arterial pressure was identical to mean intraaortic pressure in all dogs. Mean renal blood flow measured by arterial flowmeter and renal blood flow determined from the weighted harmonic means of ⁸¹Kr-washout data (F) decreased only 5–7 per cent during CPPV, a statistically insignificant reduction. There was close agreement between renal arterial flowmeter measurements and weighted harmonic mean flows from ⁸¹Kr-washout curves described by the regression line \(\bar{F} = 0.922 Q_{ra} + 27.6\) (r = 0.89, n = 50). The percentage of cardiac output required to perfuse the right kidney (Qra/Qr) increased from 7.8 to 10.0 per cent during CPPV as renal blood flow was maintained despite the fall in cardiac output. Changes in total renal vascular resistance (Rk) varied from dog to dog. Total renal vascular resistance decreased in seven of ten dogs and rose in the other three. For the group of ten dogs mean Rk decreased slightly from 0.39 ± 0.02 mm Hg/ml/min/100 g tissue to 0.37 ± 0.02 mm Hg/ml/min/100 g tissue (N.S.). Although total renal blood flow was almost unchanged by the application of PEEP, urinary output (U.O.) decreased 43 per cent.
TABLE 2. Effects of CPPV on Intrarenal Blood Flow in Ten Dogs (Mean ± SE)*

<table>
<thead>
<tr>
<th></th>
<th>F₁ (ml/min/100 g)</th>
<th>F₂ (ml/min/100 g)</th>
<th>A₁ (Per Cent)</th>
<th>A₂ (Per Cent)</th>
<th>V₁ (Per Cent)</th>
<th>V₂ (Per Cent)</th>
<th>F (ml/min/100 g Kidney)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPPV</td>
<td>472 ± 28</td>
<td>97 ± 5</td>
<td>88 ± 1</td>
<td>7 ± 1</td>
<td>74 ± 1</td>
<td>26 ± 1</td>
<td>377 ± 14</td>
</tr>
<tr>
<td>CPPV</td>
<td>470 ± 32</td>
<td>115 ± 5</td>
<td>84 ± 1</td>
<td>11 ± 1</td>
<td>67 ± 1</td>
<td>33 ± 1</td>
<td>337 ± 17</td>
</tr>
<tr>
<td>P†</td>
<td>N.S.</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.005</td>
<td>&lt;0.005</td>
<td>N.S.</td>
<td></td>
</tr>
</tbody>
</table>

* F₁ = flow rate in compartment I; F₂ = flow rate in compartment II; A₁ = per cent total renal blood flow in compartment I; A₂ = per cent total renal blood flow in compartment II; V₁ = per cent renal volume in compartment I; V₂ = per cent renal volume in compartment II; F = mean total renal blood flow.
† P values from paired Student’s t test.

There was no significant difference between the urinary outputs of the right and left ureteral catheters. Mean values ± SE for arterial hematocrit (46 ± 1 percent), pH (7.37 ± 0.01), Pco₂ (37 ± 1 mm Hg), and temperature (37.1 ± 0.4 C) did not vary significantly throughout the studies of this group of ten dogs.

Redistribution of intrarenal blood flow occurred during CPPV (table 2). The mean flow rate in compartment I (F₁) was unchanged, but the percentage of total renal blood flow to compartment I (A₁) and the percentage of renal volume occupied by compartment I (V₁) were slightly but significantly less during CPPV. Concurrently, in compartment II, CPPV led to increases in the mean flow rate (F₂), the percentage of total renal blood flow (A₂), and the percentage of renal volume (V₂). The redistribution of intrarenal blood flow did not appear to be related in any consistent manner to changes in total renal vascular resistance. The changes in cardiac index, fraction of cardiac output perfusing the right kidney, urinary output, and the intrarenal pattern of blood flow associated with CPPV were reversible and reproducible throughout the five-hour duration of each experiment (fig. 1).

CREATININE CLEARANCE AND SODIUM EXCRETION

The effects of CPPV on renal sodium excretion and creatinine clearance are summarized in table 3. In this group of ten dogs, continuous positive-pressure ventilation with 10 cm H₂O PEEP resulted in a 39 per cent decrease in urinary output, a 23 per cent decrease in creatinine clearance, and a 63 per cent decrease in urine sodium excretion, while fractional reabsorption of sodium increased. Mean intra-aortic pressure decreased slightly, from 156 ± 3 mm Hg to 150 ± 4 mm Hg (N.S.), and Pco₂ increased from 8.9 ± 1.0 cm H₂O to 14.6 ± 1.0 cm H₂O with CPPV (P < 0.001). Arterial hematocrit (45 ± 1 percent), blood pH (7.35 ± 0.01), Pco₂ (37 ± 1 mm Hg) and temperature (37.0 ± 0.3 C) were stable. The changes in sodium excretion and creatinine clearance associated with CPPV were

TABLE 3. Effects of CPPV on Sodium and Creatinine Clearance in Ten Dogs (Means ± SE)

<table>
<thead>
<tr>
<th></th>
<th>Cardiac Index (CI) (l/min/m²)</th>
<th>Urinary Output (ml/min)</th>
<th>Creatinine Clearance (Ccr) (ml/min)</th>
<th>UNa⁺ (μEq/min)</th>
<th>FNa⁺ (Per Cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPPV</td>
<td>3.69 ± 0.23</td>
<td>0.37 ± 0.03</td>
<td>56 ± 4</td>
<td>42 ± 8</td>
<td>99.49 ± 0.01</td>
</tr>
<tr>
<td>CPPV</td>
<td>2.57 ± 0.18</td>
<td>0.22 ± 0.03</td>
<td>43 ± 3</td>
<td>15 ± 2</td>
<td>99.72 ± 0.01</td>
</tr>
<tr>
<td>P†</td>
<td>&lt;0.001</td>
<td>&lt;0.002</td>
<td>&lt;0.001</td>
<td>&lt;0.005</td>
<td>&lt;0.002</td>
</tr>
</tbody>
</table>

* UNa⁺ = urinary sodium excretion.
† FNa⁺ = fractional reabsorption of Na.
† P values from paired Student’s t test.
reproducible throughout the five-hour experiment (fig. 2).

**RENAL HEMODYNAMICS, CREATININE CLEARANCE, AND SODIUM EXCRETION**

Simultaneous measurements of renal hemodynamics, creatinine clearance, and sodium excretion obtained in four dogs are presented in figure 3. CPPV resulted in decreases in the percentage of renal volume in compartment I from 74 ± 2 to 66 ± 3 per cent ($P < 0.05$), in urinary output from $0.47 ± 0.07$ ml/min to $0.28 ± 0.05$ ml/min ($P < 0.05$), creatinine clearance from $62.4 ± 4.4$ ml/min to $44.6 ± 4.2$ ml/min ($P < 0.05$), and sodium excretion from $50 ± 1$ μEq/min to $14 ± 1$ μEq/min ($P < 0.05$). Mean fractional reabsorption of sodium increased from $99.43 ± 0.10$ per cent to $99.74 ± 0.07$ per cent ($P < 0.05$), while renal arterial blood flow did not change significantly ($208 ± 16$ ml/min versus $196 ± 20$ ml/min).

**Discussion**

Previous investigators have observed a 30 per cent decrease in effective renal plasma flow (ERPF) estimated by PAH techniques in man during continuous positive-pressure breathing with $32$ cm H$_2$O PEEP$^2$ and a 50 per cent decrease in ERPF in dogs during continuous positive-pressure ventilation with $15$ cm H$_2$O PEEP$^3$. More recently, Tucker and Murray$^4$ found no change in renal arterial-venous differences in O$_2$ content in dogs ventilated with $10$ cm H$_2$O PEEP and concluded that no significant change in renal blood flow occurred during PEEP. The present study also suggests that total renal blood flow is not significantly changed in dogs ventilated with $10$ cm H$_2$O PEEP. Despite a 29 per cent decrease in cardiac index, total renal perfusion as measured by two independent techniques remained essentially unchanged. The discrepancy between the observations of Baratz and Ingham$^5$ and our findings is probably related in part to the lower PEEP used in the present studies, but the difference may also be
related to the techniques used to assess renal perfusion. Estimation of renal plasma flow by measuring PAH clearance as used by earlier investigators may not accurately reflect total renal perfusion during antidiuresis or in physiologic states associated with altered intrarenal distribution of blood flow. In the presence of low urine-flow rates, medullary nephron loops may reabsorb PAH from the urine. This would lead to falsely low estimates of renal plasma flow. Furthermore, since PAH extraction occurs primarily in the renal cortex and not in medullary tissue, a relative increase in perfusion of juxtedudillary tissue (as represented by compartment II in our Kr-washout studies) would also lead to falsely low estimates of renal plasma flow.

The role of intrinsic renal autoregulatory mechanisms in preserving total renal perfusion during CPPV is unclear. Although the application of 10 cm H2O PEEP caused a 29 percent decrease in cardiac index, mean renal arterial pressure fell only 9 mm Hg, demonstrating the capacity of the dog's cardiovascular system to maintain central arterial pressure in the face of a moderately compromised cardiac output. The stability of renal arterial perfusion pressure may account for the relative constancy of total renal blood flow. However, the slight decrease in calculated total renal resistance observed in seven of the ten dogs studied for renal hemodynamics suggests that changes in total renal vascular tone may occur during PEEP. The integrated action of the various cardiovascular and renal homeostatic mechanisms mobilized in response to decreases in cardiac output and intrathoracic blood volume present during CPPV result in delivery to the kidneys of a larger fraction of the cardiac output. Total renal blood flow is maintained at the expense of the perfusion of other vascular beds, such as the portal splanchnic system and the extremities.

Although total renal blood flow remains essentially unchanged during ventilation with 10 cm H2O PEEP, 82Kr-washout data demonstrate that the distribution of intrarenal blood flow is altered significantly. With the application of 10 cm H2O PEEP, the percentage of renal blood flow perfusing the outer cortex decreases slightly, while blood flow to the juxtedudillary region increases. As perfusion of the juxtedudillary zone increases, the fractional reabsorption of sodium increases and urinary sodium excretion decreases. Similar changes in the pattern of intrarenal perfusion have been shown by 82Kr- or 133Xe-washout techniques and autoradiography to be present in a variety of conditions associated with sodium retention (with or without significant changes in cardiac output), such as congestive heart failure, hemorrhage, stimulation of the renal sympathetic nerves, partial occlusion of the thoracic inferior vena cava, early renal allograft rejection, and low-sodium diets. The association between increased juxtedudillary blood flow and sodium retention during CPPV in dogs is compatible with the physiologic differences of outer and inner cortical nephrons found by Horster and Thura in rats. Micropuncture studies of
single-nephron glomerular filtration rates revealed a redistribution of glomerular filtration during states of sodium deprivation from outer cortical nephrons to juxtaglomerular nephrons without large changes in the total renal glomerular filtration rate, suggesting that juxtaglomerular nephrons were more efficient in conserving sodium. Although the decrease in total renal glomerular filtration rate measured in our studies may account for some of the observed decrease in urinary sodium excretion, the redistribution of blood flow to juxtaglomerular nephrons with greater sodium-conserving capacity may also contribute to the sodium retention seen during CPPV.

Decreases in glomerular filtration rate during CPPV were believed previously to be secondary to concomitant reductions in total renal perfusion.\textsuperscript{1,2,3} However, the present studies revealed a marked dissociation between a marginal reduction in renal arterial blood flow and a 23 per cent decrease in glomerular filtration rate and a 63 per cent decrease in urinary sodium excretion. Although the small decrease in total renal blood flow may account for part of the disproportionately large decline in glomerular filtration and sodium excretion, other mechanisms must be involved. When renal arterial pressure is directly varied by graded occlusion of the aorta or renal artery, dissociation between renal perfusion and glomerular filtration rate has been demonstrated in dogs and rats, but only when mean renal arterial pressure falls below 100 mm Hg.\textsuperscript{29} The dissociation observed in the present studies occurred with mean renal arterial pressures between 130 and 180 mm Hg in kidneys responding through presumably intact neurohormonal pathways to significant decreases in intrathoracic blood volume and cardiac output caused by a sustained increase in intrathoracic pressure. Although manipulation of the renal artery is known to alter renal autonomic control of both vascular tone and function, the fact that the manipulated and non-manipulated kidneys behaved similarly with regard to urinary output suggests that the kidneys in our studies were relatively unaffected by the surgical procedures. The physiologic responses of kidneys to barostatic neurohormonal reflexes mobilized to support central arterial pressure and renal blood flow in the face of falling intrathoracic blood volume and cardiac output undoubtedly differ from the renal vascular responses to direct occlusion of the renal blood supply.

Robertson et al.\textsuperscript{29} found that the changes in intravascular volume could alter the relationship between glomerular plasma flow and glomerular filtration rate in rats by altering the balance of afferent and efferent arteriolar resistances. The decreases in intrathoracic blood volume and cardiac index present in dogs during CPPV may cause similar changes in afferent and efferent arteriolar tone. Neurohormonal mechanisms involved in the redistribution of intrarenal blood flow have been shown to have different effects on the afferent and efferent arterioles. Adrenergic nerve terminals are present on afferent but not efferent arterioles in dogs.\textsuperscript{29} Mild stimulation of the renal nerves\textsuperscript{21} or intra-arterial infusion of norepinephrine\textsuperscript{a} results in decreased perfusion of outer cortical glomeruli and peritubular capillaries, suggesting the presence of afferent arteriolar constriction. Antidiuretic hormone\textsuperscript{20} and angiotensin\textsuperscript{25} have been implicated as regulators of efferent arteriolar tone. Alterations in sympathetic tone and circulating vasoactive hormones present during CPPV could lead, therefore, to a redistribution of intrarenal blood flow and to decreases in glomerular filtration pressure and GFR without significant change in total renal blood flow.

Whether or not the changes observed in the distribution of intrarenal blood flow, sodium excretion, and creatinine clearance during CPPV could be reversed by transfusing the dogs back to cardiac indices present during IPPV is unresolved and merits further study. It is difficult to speculate which, if any, of the many neurohormonal factors involved in the control of renal perfusion and function would be returned to control levels by transfusing the dogs during ventilation with 10 cm H\textsubscript{2}O PEEP into a hypervolemic state with the elevated right-sided cardiac filling pressures necessary to restore pre-CPPV cardiac indices. Redistribution of intrarenal perfusion and decreases in sodium excretion similar to those we observed have been demonstrated in dogs with thoracic inferior vena caval pressures elevated to 8–14 cm H\textsubscript{2}O. However, subhepatic inferior vena caval occlusion with
femoral-vein pressures similarly elevated to 8–14 cm H2O led to no demonstrable change in renal hemodynamics or function, raising the possibility of hepatorenal reflexes which might influence renal perfusion and sodium excretion in response to elevated hepatic-vein pressures. Unfortunately, cardiac indices and superior vena caval pressures were not measured.

Sodium pentobarbital has been reported to depress renal hemodynamics and sodium excretion in innervated dog kidneys. However, we found no significant depression of either renal hemodynamics or function in dogs ventilated with IPPV. Baseline total renal blood flows and intrarenal distribution of blood flows during IPPV were closely comparable to those found in unanesthetized dogs. Baseline creatinine clearances and sodium excretions were essentially identical to those found in unanesthetized dogs.

Neurohormonal responses to decreases in intrathoracic blood volume and cardiac index include increased sympathetic tone and catecholamine release, release of antidiuretic hormone, and activation of the renin–angiotensin system. Each of these individual components has been shown to have its own effect on renal vasculature and sodium and water excretion. The net balance of the numerous interacting neurohormonal mechanisms involved in supporting central arterial pressure during CPPV with 10 cm H2O PEEP results in a marked reduction in renal sodium and water excretion associated with changes in intrarenal distribution of blood flow and a marginal decrease in total renal blood flow. Alterations in the balance of afferent and efferent arteriolar tone and redistribution of blood flow from outer cortical nephrons to juxtamedullary nephrons play central roles in the complex pathophysiology of the sodium and water retention seen during continuous positive-pressure ventilation.

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References