Factors Involved in the Antinatriuretic Effects of Acute Constriction of the Thoracic and Abdominal Inferior Vena Cava

By Robert W. Schrier and Michael H. Humphreys

With the Technical Assistance of Judith A. Harbottle

ABSTRACT

Studies were performed on anesthetized saline-loaded dogs to delineate the factors involved in the antinatriuretic effect of acute constriction of the thoracic (TIVC) and abdominal (AIVC) inferior vena cava. Acute TIVC constriction lowered cardiac output and arterial blood pressure and reduced urinary sodium excretion 48%; the same degree of reduction in renal perfusion pressure by suprarenal aortic constriction diminished sodium excretion only 27%. This finding suggested that factors other than a reduction in renal perfusion pressure are involved in the antinatriuretic effect of acute TIVC constriction. This conclusion was confirmed by studies in which a significant antinatriuretic effect (23%) was observed during acute TIVC constriction while renal perfusion pressure and renal venous pressure were held constant. A similar degree of constriction of the AIVC, as judged by the increase in vena cava pressure, did not cause a decrease in arterial pressure or cardiac output, and the modest antinatriuretic effect of this maneuver was not observed when renal venous pressure was held constant. The antinatriuretic effect of TIVC constriction which occurred in the absence of changes in renal perfusion pressure and renal venous pressure did not correlate with alterations in renal vascular resistance, glomerular filtration rate, and calculated initial postglomerular protein concentration and was not abolished by renal denervation or adrenalectomy. The afferent stimulus for the antinatriuretic effect may be related to the alterations in systemic hemodynamics which occur during acute TIVC, but not AIVC, constriction.

KEY WORDS
renal venous pressure
sodium excretion
renal arterial pressure
renal vascular resistance
anesthetized dog

The factors involved in the sodium retention associated with low output cardiac failure have not been well delineated. Several investigators have used acute constric-

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above the entrance of the renal veins does not abolish the natriuretic effect of a saline infusion (1). Although the effect of a comparable degree of AIVC constriction is unknown, several investigators have demonstrated that acute TIVC constriction is associated with a decrease in arterial pressure (2, 4-6). Since alterations in renal perfusion pressure affect sodium reabsorption (7-9), the decrease in renal perfusion pressure during acute TIVC constriction may be a factor in the resulting antinatriuresis. The results of two recent investigations have provided some evidence in support of this possibility (2, 4). Earley et al. (2) have demonstrated that fractional sodium reabsorption in the proximal tubules decreases when the decreased arterial pressure resulting from TIVC constriction is returned to control levels by the infusion of norepinephrine or angiotensin. More recently, Friedler and associates (4) have demonstrated that acetylcholine-induced renal vasodilatation combined with angiotensin- or norepinephrine-induced increases in systemic arterial pressure can return sodium excretion during saline infusion to normal control levels despite continued constriction of the TIVC.

The present study examines the antinatriuretic effect of acute TIVC constriction in the absence of alterations in renal perfusion pressure and compares the effects of equivalent degrees of TIVC and AIVC constriction on arterial pressure, renal hemodynamics, and electrolyte excretion.

Methods

Experiments were performed on mongrel dogs of either sex weighing 20-30 kg. Two of the animals had undergone adrenalectomy approximately 1 week prior to study and received 25 mg of hydrocortisone every 12 hours and 5 mg of deoxycorticosterone acetate daily from the time of surgery up to and including the day of the experiments. All animals had free access to water, but food was withheld beginning 18 hours before the experiment. On the day of the experiment, the animals were anesthetized with pentobarbital (30 mg/kg, iv) and ventilated automatically through an endotracheal tube connected to a Harvard respirator. Light anesthesia (judged by preservation of corneal reflexes) was maintained throughout the experiment by intermittent administration of pentobarbital. Pitressin taonate in oil, 2.5 units, and deoxycorticosterone acetate, 5 mg, were injected intramuscularly 4-6 hours prior to the experiment. In 17 animals, a polyethylene snare was placed around the TIVC through a right thoracotomy incision. In seven animals, four of which had thoracic snares, a snare was placed around the AIVC just above the entrance of the renal veins. Plastic catheters were inserted through bilateral retroperitoneal flank incisions into each ureter and into both renal veins for a distance of 2-3 cm. In eight dogs, including the two that had adrenalectomy, the left renal pedicle was denervated and, in most of these animals, a 95% alcohol solution also was applied to the left renal artery to ensure denervation. A Blalock clamp was placed around the aorta above both renal arteries (nine dogs) or between the renal arteries (eight dogs) to allow either bilateral or unilateral control of renal perfusion pressure. In six dogs, a loop of polyethylene catheter or umbilical tape was placed around the left renal vein to allow the unilateral elevation of the left renal venous pressure. Polyethylene catheters were inserted into the inferior vena cava, brachial artery, and the aorta (below the level of the Blalock clamp). Venous pressure was measured in the inferior vena cava below the entrance of the renal veins in all experiments. Bilateral renal venous pressures were measured through the catheters in the renal veins in those experiments in which unilateral renal vein constriction was performed. Venous, aortic, and brachial artery pressures were measured continuously with pressure transducers connected to a direct-writing recorder (Hewlett-Packard). A catheter was also inserted into the jugular vein to inject indocyanine dye; cardiac output was determined by the dye dilution method with a Gilson densitometer and a Lexington Instruments cardiac output computer. After the surgical procedures, isotonic saline was infused at a rate of 0.5 ml/min through each renal vein catheter; saline (0.5 ml/min) containing sufficient insulin to maintain blood levels of this substance between 15 and 25 mg and sufficient para-aminohippuric acid (PAH) to maintain blood levels between 1 and 3 mg was also infused intravenously. Aqueous Pitressin (50 mU/kg hr-1) was also added to the maintenance infusion. At the same time, an infusion of Ringer’s solution was started at a rate of 15-20 ml/min and continued for 90 minutes and then decreased to a rate 4-6 ml/min greater than urine flow. The experiment was started when the urine flow rate had stabilized. During the experiment, urine was collected at 5-minute intervals, and arterial and renal vein blood samples were collected at the midpoint of alternate collections of urine.
measurements were also made during the same alternate periods in which the blood samples were drawn. Experiments were performed according to the following protocols.

**ACUTE CONSTRICTION OF THE THORACIC OR ABDOMINAL INFERIOR VENA CAVA**

In 16 animals, the TIVC was constricted acutely to produce a mean rise in venous pressure of 5 mm Hg below the constriction. In these experiments, 3-5 control urine and blood samples were obtained, then the TIVC was constricted. After an equilibration period of 10-15 minutes, 3-5 experimental samples were obtained as the TIVC constriction was maintained. The TIVC constriction was then released, and after another 10- to 15-minute equilibration period, 3—5 postconstriction control samples were collected. In eight animals the same protocol was followed except that the AIVC was constricted to increase the mean venous pressure by 5 mm Hg below the constriction. In some instances, experiments involving constriction of the TIVC and the AIVC were performed on the same animal.

**ACUTE CONSTRICTION OF THE THORACIC VENA CAVA WITHOUT ALTERATION OF RENAL PERFUSION PRESSURE OR RENAL VENOUS PRESSURE**

In 14 animals, perfusion pressure of the left or both kidneys was kept constant by adjusting a Blalock clamp. In eight of these animals, a snare was also placed around the left renal vein to control left renal venous pressure as described above. In the experiments in which the aortic clamp was placed between the renal arteries, the right kidney served as a control. The protocol in these experiments was as follows: after 3-5 control urine samples were collected, renal perfusion pressure was lowered by aortic constriction by a mean of 26 mm Hg, a decrement similar to that which occurred with acute TIVC constriction. After a 10- to 15-minute equilibration period, 3—5 control samples were collected and then the TIVC was constricted acutely to increase the venous pressure below the clamp by a mean of 5 mm Hg. As the TIVC was constricted, the aortic clamp was adjusted to maintain renal perfusion pressure constant. Experimental samples were collected at the same perfusion pressure as during the control periods. The postconstriction control urine samples were also obtained at a constant renal perfusion pressure by adjusting the aortic clamp. In six of the same animals, renal perfusion pressure was decreased and left renal venous pressure was increased before control urine samples were obtained. In these animals, both renal perfusion pressure and renal venous pressure were held constant as the TIVC was constricted acutely and released as described above. Otherwise the protocol of the experiments was the same as that described above.

**ACUTE CONSTRICTION OF THE ABDOMINAL INFERIOR VENA CAVA WITHOUT ALTERATION OF RENAL VENOUS PRESSURE**

In four kidneys in three animals, the renal venous pressure (RVP) was held constant as described above, and control urine samples were obtained during AIVC constriction and release.

Analytical procedures have been described previously (10). Renal plasma flow (RPF) was calculated from the formula of Wolf (11): RPF = V(U - R)/(A - R), where V = rate of urine flow and U = urinary concentration, R = renal vein concentration, and A = arterial concentration of PAH. Renal blood flow (RBF) was calculated as RPF/(1 - Hct). Renal vascular resistance (mm Hg/ml min⁻¹) was calculated as (MABP - RVP)/RBF, where MABP = mean arterial blood pressure. Filtration fraction (FF) was calculated as glomerular filtration rate divided by renal plasma flow. Initial postglomerular protein concentration (PGP) was calculated by the formula of Bresler (12) where PGP = PP/(1 FF), where PP is plasma protein concentration.

![FIGURE 1](http://circres.ahajournals.org/)

**FIGURE 1**

Effect of acute constriction of the thoracic and abdominal inferior vena cava on cardiac output and total peripheral resistance. Each symbol represents the mean value of at least two determinations in one animal for paired groups of control and experimental measurements. The 45° line is the line of no change; values which increased during the experiment lie above this line and values which decreased lie below this line.
TABLE 1

Effects of Acute Constriction of the Thoracic and Abdominal Inferior Vena Cava on Systemic and Renal Hemodynamics and Sodium Excretion

<table>
<thead>
<tr>
<th></th>
<th>TIVC (24)*</th>
<th>AIVC (15)*</th>
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<td></td>
<td>Mean ± SE</td>
<td>P</td>
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</table>

CO (liters/min)
- Control: 3.4, 0.14
- Constriction: 2.3, 0.08
- Release: 3.4, 0.14

MABP (mm Hg)
- Control: 149, 5.3
- Constriction: 121, 4.7
- Release: 148, 8.5

TPR (dyne sec cm⁻¹)
- Control: 3543, 222
- Constriction: 4177, 203
- Release: 3500, 217

IVCP (mm Hg)
- Control: 6.7, 0.5
- Constriction: 10.6, 0.6
- Release: 6.2, 0.5

GFR (ml/min)
- Control: 51.7, 3.6
- Constriction: 46.3, 3.7
- Release: 51.1, 3.3

RBF (ml/min)
- Control: 250, 14.4
- Constriction: 216, 15.0
- Release: 251, 17.0

RVR (mm Hg/ml min⁻¹)
- Control: 0.630, 0.055
- Constriction: 0.688, 0.057
- Release: 0.653, 0.065

FF
- Control: 0.298, 0.013
- Constriction: 0.320, 0.013
- Release: 0.303, 0.014

U₅V (µEq/min)
- Control: 492, 53
- Constriction: 227, 24
- Release: 458, 52

UₑV (µEq/min)
- Control: 83, 4.6
- Constriction: 64, 3.3
- Release: 77, 3.7

Total peripheral resistance was calculated in only ten animals in the thoracic group because of the presence of an aortic clamp above one renal artery.

CO = cardiac output; MABP = mean arterial blood pressure; TPR = total peripheral resistance; IVCP = inferior vena cava pressure; GFR = glomerular filtration rate; RBF = renal blood flow; RVR = renal vascular resistance; FF = filtration fraction; U₅V = urinary sodium excretion; UₑV = urinary potassium excretion; TIVC = thoracic inferior vena cava; AIVC = abdominal inferior vena cava.

*Renal hemodynamics and electrolyte measurements were made on 24 kidneys from 14 animals for the TIVC experiments and 15 kidneys from 8 animals for the AIVC experiments.

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Results

EFFECTS OF ACUTE CONSTRICTION OF THE THORACIC INFERIOR VENA CAVA

Acute constriction of the TIVC lowered cardiac output from 3.4 to 2.3 liters/min and caused a fall in blood pressure from 149 to 121 mm Hg (Fig. 1). Venous pressure below the snare rose from 7 to 11 mm Hg, and total peripheral resistance increased from 3543 to 4177 dyne sec cm⁻². Each of these significant changes returned to control values on release of the TIVC constriction (Table 1). Glomerular filtration rate fell slightly, but significantly, from 52 to 48 ml/min (P<0.02) in response to TIVC constriction. Renal blood flow was also decreased by acute constriction of the TIVC and returned to the control value on release of the constriction, as did glomerular filtration rate. Renal vascular resistance did not change significantly when the TIVC was constricted but rose slightly as the constriction was released. The filtration fraction was significantly elevated by acute constriction and returned to its control value on release.

Arterial concentration of plasma protein decreased from 4.7 to 4.4 g/100 ml plasma during TIVC constriction, so that the calculated initial postglomerular protein concentration changed only minimally from 6.7 to 6.5 g/100 ml.

These alterations in systemic and renal hemodynamics were associated with significant changes in electrolyte excretion. Urinary sodium excretion (Uₙₐᵥ) decreased from a mean of 492 to 227 μEq/min on constriction of the TIVC and returned to 458 μEq/min on release. Similarly, urinary potassium excretion (Uₖᵥ) fell from a mean of 83 to 64 μEq/min on constriction and rose again to 77 μEq/min as constriction was released. These changes in electrolyte excretion were all highly significant (Table 1). In 8 denervated kidneys, Uₙₐᵥ fell from 525 to 242 μEq/min on constriction of the TIVC and rose to 426 μEq/min on release, while in 15 innervated kidneys the corresponding numbers were 440, 211, and 435 μEq/min, respectively. Although the control Uₙₐᵥ was higher in the denervated kidneys, the changes in Uₙₐᵥ following constriction or release of the TIVC were not significantly different for innervated and denervated kidneys. When results from groups of animals were compared, the nonpaired Student's t-test was used; but when the same animal served as its own control, the paired t-test was used for statistical analysis.

EFFECTS OF DIMINISHING ARTERIAL PRESSURE BY AORTIC CONSTRICTION ON RENAL HEMODYNAMICS AND SODIUM EXCRETION

Renal perfusion pressure was lowered by constriction of the aorta with a Blalock clamp placed above the left or both kidneys from a mean of 147 to 121 mm Hg, a decrement similar to that occurring during TIVC constriction. This degree of aortic constriction caused a slight but significant fall in cardiac output (3.8 to 3.4 liters/min, P<0.01), but inferior vena cava pressure was not altered. Total peripheral resistance was not calculated because of the different arterial pressures above and below the aortic clamp. Glomerular filtration rate was not significantly different before and during aortic constriction (57.5 and 57.4 ml/min, respectively), and renal blood flow was 284 ml/min before and 249 ml/min (P<0.001) after aortic constriction. Renal vascular resistance decreased significantly from 0.56 to 0.52 mm Hg/ml min⁻¹ (P<0.02) and the filtration fraction increased significantly from 0.30 to 0.33 (P<0.001) during aortic constriction. At the same time, the plasma protein concentration decreased from 4.45 to 4.25 g/100 ml. Calculated initial peritubular protein concentration was 6.36 g/100 ml before aortic constriction and 6.34 g/100 ml after aortic constriction. The renal hemodynamic changes resulting from aortic constriction were associated with a 27% decrease in Uₙₐᵥ (from 610 to 448 μEq/min, P<0.001), in contrast to the 48% decrease (492 to 277 μEq/min) found during the same diminution in arterial pressure caused by acute constriction of the TIVC. When the decrements in Uₙₐᵥ during TIVC constriction were compared with the decrements in Uₙₐᵥ during aortic constriction, the difference was significant (P<0.025). Uₖᵥ also diminished significantly during aortic constriction from 99 to 84 μEq/min (P<0.001). Release of the
aortic constriction at the end of the experiments was associated with a reversal of these changes in renal hemodynamics and electrolyte excretion.

**EFFECTS OF ACUTE CONSTRUCTION OF THE THORACIC INFERIOR VENA CAVA WITHOUT ALTERATION IN RENAL PERFUSION PRESSURE**

Two groups of studies were performed in which the TIVC was constricted and renal perfusion pressure maintained constant by adjustment of an aortic clamp. In group 1 only renal perfusion pressure was controlled and in group 2 both renal perfusion and renal venous pressure were controlled. The effect of acute TIVC constriction on cardiac output, arterial blood pressure, and venous pressure was the same as in the initial group of studies. The mean values for the alterations in systemic hemodynamics in groups 1 and 2 are shown in Table 2. Acute TIVC constriction was not associated with a significant change in renal blood flow or glomerular filtration rate in either group 1 or group 2. Figure 2 shows that acute TIVC constriction may decrease $U_{Na}V$ in the absence of changes in glomerular filtration rate, renal vascular resistance, and calculated postglomerular protein concentration when renal venous and arterial blood pressures are unchanged. The animal used in this experiment had an adrenalectomy a week before experimentation, and the kidney was denervated on the day of the experiment. In 13 denervated kidneys in groups 1 and 2, mean $U_{Na}V$ fell from 378 to 243 μEq/min after TIVC constriction, and increased to 348 μEq/min after release of constriction. In 6 innervated kidneys in the same groups, $U_{Na}V$ fell from 379 to 245 μEq/min on constriction and rose to 433 μEq/min on release. In these groups, control $U_{Na}V$ was not significantly different, thus the effect of the denervation on $U_{Na}V$ may have then been obscured by the saline loading. The renal venous extraction of PAH in the experiments on group 1 was 0.926 before and 0.906 after TIVC constriction. In the group 2 experiments the renal venous extraction of PAH was 0.810 and 0.821, respectively, before and after TIVC constriction. In neither group were these changes significantly different. Neither the filtration fraction nor renal vascular resistance was significantly altered by TIVC constriction or release in group 1 or group 2. Acute constriction of the TIVC was consistently associated with changes in $U_{Na}V$ in both groups 1 and 2 (Table 2). However, the degree of diminution in $U_{Na}V$ was most marked in group 1 where changes in renal venous pressure were not controlled. In group 2, $U_{Na}V$ decreased in six of eight kidneys during acute TIVC constriction ($P < 0.025$) and increased in eight of eight kidneys on release of the constriction ($P < 0.005$). When the decrements in $U_{Na}V$ during TIVC constriction without control of renal perfusion pressure or renal venous pressure (Table 1) were compared with the decrements during TIVC constriction with control of these parameters (Table 2), the difference was highly significant ($P < 0.005$). No significant difference occurred in the decrease in $U_{Na}V$ following TIVC constriction which was observed in each group.

**FIGURE 2**

*Effect of acute constriction of the thoracic inferior vena cava on sodium excretion in the absence of changes in renal arterial and venous pressure. The study was performed in an adrenalectomized animal receiving exogenous mineralocorticoid, and the animal’s kidneys were denervated before the study.*

Circulation Research, Vol. XXIX, November 1971
Effects of Acute Constriction of the Thoracic Inferior Vena Cava without Alterations in Renal Perfusion or Renal Venous Pressure on Systemic and Renal Hemodynamics and Sodium Excretion

**TABLE 2**

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<th>RPP (mm Hg)</th>
<th>RVP (mm Hg)</th>
<th>GFR (ml/min)</th>
<th>RBF (ml/min)</th>
<th>RVR (mm Hg/ml min⁻¹)</th>
<th>FF</th>
<th>UN.V (mEq/min)</th>
<th>UKV (mEq/min)</th>
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SABP = systemic arterial blood pressure; RPP = renal perfusion pressure; RVP = renal venous pressure; all other abbreviations are the same as in Table 1.
×In two animals the RPP was controlled in both kidneys and in four animals only in the left kidney for a total of eight kidneys.
†In three animals the RPP and RVP were controlled in both kidneys and in five animals only in the left kidney for a total of 11 kidneys.

**EFFECTS OF ACUTE CONSTRICTION OF THE ABDOMINAL INFERIOR VENA CAVA**

Acute constriction of the AIVC was associated with an increase in venous pressure from 7 to 12 mm Hg, a change comparable to that seen during TIVC constriction. However, this degree of AIVC constriction did not
Absence of Effects of Acute Constriction of the Abdominal Inferior Vena Cava when Renal Venous Pressure Is Held Constant

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Abbreviations are the same as in Table 1. NS = P > 0.5 with paired Student's t-test.

EFFECTS OF ELEVATING RENAL VENOUS PRESSURE BY RENAL VEIN CONSTRICTION ON RENAL HEMODYNAMICS AND SODIUM EXCRETION

In ten animals, constriction of the left renal vein increased left renal venous pressure from 10 to 16 mm Hg. This increment was similar to that which occurred during acute constriction of the TIVC and the AIVC. This unilateral increase in renal venous pressure had no significant effect on systemic hemodynamics. Renal hemodynamics were also not significantly altered: glomerular filtration rate was 61 ml/min before and 62 ml/min after and renal blood flow was 278 before and 277 ml/min after elevation of renal venous pressure. Renal vascular resistance decreased from 0.45 to 0.44 mmHg/ml min⁻¹ and the filtration fraction increased from 0.31 to 0.32 after venous constriction. These changes were not significantly different. Elevation in renal venous pressure was associated with a 14% decrease in UrNaV (from 467 to 401 µEq/min, P < 0.005), but no significant change in UrK (97 to 94 µEq/min) resulted. When the decrements in UrNaV during AIVC constriction were compared with the decrements during renal vein constriction, the difference was not significant (P < 0.4). At the end of the experiments, release of renal vein constriction was associated with a reversal of the changes in renal hemodynamics and electrolyte excretion.

EFFECTS OF ACUTE CONSTRICTION OF THE ABDOMINAL INFERIOR VENA CAVA WITHOUT ALTERATION OF RENAL VENOUS PRESSURE

The results of acute constriction of the abdominal inferior vena cava at a constant renal venous pressure are shown in Table 3. In these studies, no consistent or significant changes were noted in either renal hemodynamics or electrolyte excretion.

Discussion

The results of the present experiment demonstrate that acute AIVC and TIVC constriction exert substantially different effects on systemic hemodynamics. The diminution in cardiac output and arterial pressure which occurs during acute TIVC, but not AIVC,
constriction may be an important factor in the different effects of these maneuvers on sodium excretion. Alternatively, the different effects of AIVC and TIVC constriction on hepatic venous pressure may be of primary importance. In a recent study (13), we have shown that the changes in cardiac output and arterial pressure, rather than the differences in hepatic vein congestion, probably initiate the pronounced antinatriuretic effect of TIVC constriction. In this study (13), a decrease in cardiac output similar to that resulting from acute TIVC constriction was produced by constriction of the superior vena cava; the antinatriuretic effect of these two maneuvers was similar, although only TIVC constriction increased hepatic venous pressure.

In the present study, acute TIVC constriction decreased cardiac output, but a previous study (14) showed that chronic TIVC constriction did not. This difference suggests that the mechanisms whereby these two maneuvers decrease $U_{\text{NaV}}$ may also be different. While the investigation of the factors involved in chronic TIVC constriction may best allow for the delineation of any compensatory mechanisms, the investigation of acute TIVC constriction may best allow for the elucidation of the events which initiate the process of sodium retention. Thus, investigation of both the acute and chronic experimental models of caval constriction may be important in understanding the pathogenesis of sodium retention.

In addition to delineating the different effects of acute AIVC and TIVC constriction on systemic hemodynamics, the present study provided information about the pathways linking caval constriction with antinatriuresis. The results suggest that the modest antinatriuretic effect of acute AIVC constriction is due to the elevation in renal venous pressure, since AIVC and renal vein constriction are quantitatively comparable for the same increase in renal venous pressure and since acute constriction of the AIVC does not diminish $U_{\text{NaV}}$ if the renal venous pressure is not allowed to increase. The decrease in renal arterial pressure which occurs during acute TIVC constriction may also be a factor in the more pronounced antinatriuretic effect of this maneuver. Earley et al. (2) and Friedler et al. (4) previously suggested that diminished arterial pressure during acute TIVC constriction contributes to the antinatriuretic effect, and an inverse relationship between renal perfusion pressure and sodium reabsorption has been demonstrated in other experiments (7-9). In the present study, the antinatriuretic effect of acute TIVC was quantitatively more pronounced in the experiments in which renal perfusion pressure was not controlled as compared to those experiments in which it was kept constant. Taken together, these findings thus support the importance of both an elevation of renal venous pressure and a diminution in renal arterial pressure in the antinatriuretic effect of acute TIVC constriction.

The results of the present study also demonstrate that factors other than renal venous and arterial pressure are involved in the antinatriuretic response to acute TIVC constriction (Fig. 2). We have also recently shown that the antinatriuretic effect associated
with acute constriction of the thoracic superior vena cava may occur in the absence of changes in either renal venous or arterial pressure (13). Since this antinatriuretic effect was demonstrable in the denervated kidney and occurred in the absence of observed changes in the physical characteristics of the blood known to affect sodium excretion, i.e., hematocrit (15) and plasma protein concentration (16, 17), the effect probably is mediated by an alteration of the concentration of a circulating substance affecting sodium excretion. The administration of supraphysiological doses of mineralocorticoid and vasopressin throughout the experiments, as well as the demonstration of the effect in the adrenalectomized dog, would seem to exclude both adrenal hormones and vasopressin as the circulating substance. Since exogenous mineralocorticoid was administered in all of the present experiments, the results are, however, compatible with the proposal of Davis et al. (18) that the presence of excess mineralocorticoids is necessary for the expression of the antinatriuretic effect.

The evaluation of glomerular filtration rate, renal vascular resistance, and the filtration fraction did not show that any humorally induced effect on sodium excretion during acute TIVC constriction was mediated by an effect on renal hemodynamics. Although Garella et al. (5) and Levinsky and Lalone (3) were unable to dissociate the antinatriuretic effect of acute TIVC constriction from changes in glomerular filtration rate, the degree of vena cava constriction in their studies was more pronounced than in the present studies, and renal perfusion pressure was not controlled. Studies with a similar severe degree of acute TIVC constriction by Cirksena et al. (1), however, suggested that factors other than alterations in glomerular filtration rate were involved. They proposed this possibility because decreases in filtration rate during aortic constriction did not abolish the depression of proximal tubule fractional reabsorption observed during a saline infusion (19). The results of the present study involving less severe acute TIVC constriction support this possibility, since the antinatriuretic effect could be demonstrated without detectable changes in filtration rate (Fig. 2).

Alterations in renal vascular resistance, the filtration fraction, and calculated initial post-glomerular protein concentration were not adequate to explain the effect of acute TIVC constriction on \( U_{\text{Na}} \). The results of Friedler et al. (4) suggested that an increase in renal vascular resistance might be involved in the antinatriuretic effect of acute TIVC constriction, since acetylcholine-induced renal vasodilatation, in addition to the pressor effect of angiotensin or norepinephrine, was necessary to increase the rate of urinary sodium excretion to control levels during sustained TIVC constriction. Alternatively, the induced renal vasodilatation may primarily have prevented the vasoconstrictor effects of the administered vasopressor agents or may have obscured the detection of other antinatriuretic factors. The latter possibility is not unlikely, since the recent results of Stein et al. (20) suggest that acetylcholine may depress proximal sodium reabsorption by a pathway independent of its effect on renal hemodynamics. Although Friedler et al. (2) did not observe an increase in renal vascular resistance during acute TIVC constriction, the simultaneous administration of saline may have obscured this effect. In the present study, however, the TIVC was acutely constricted after sustained volume expansion and natriuresis had been achieved; detectable and reversible increases in renal vascular resistance were also not observed.

The possibility that the effect of acute TIVC constriction on sodium excretion may involve a humorally mediated redistribution in renal blood flow has been suggested by Kilcoyne and Cannon (21, 22). Newsome et al. (23) have also suggested that the sodium retention associated with chronic cava constriction may involve alterations in the intrarenal distribution of blood flow. Alternatively, however, the effect of acute TIVC constriction on tubular sodium reabsorption may be mediated by a humoral substance directly affecting sodium transport independent of any simultaneous
alterations in the intrarenal redistribution of blood flow.

References


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Factors Involved in the Antinatriuretic Effects of Acute Constriction of the Thoracic and Abdominal Inferior Vena Cava
Robert W. Schrier and Michael H. Humphreys

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