Role of the Sympathetic Nervous System in the Renal Response to Hemorrhage

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ABSTRACT In 12 studies, a femoral artery and vein of a donor dog treated with desoxycorticosterone were connected by tubing to a renal artery and vein of a recipient dog treated with desoxycorticosterone, and the kidney with its nerve supply intact was perfused at femoral arterial pressure. Infusion of normal saline, which contained albumin, from 2.7 to 3.1 g/100 ml, in the donor produced significant natriuresis in a kidney of the donor (from 112 to 532 μEq/min) and in the perfused kidney (from 60 to 301 μEq/min) of the recipient. Increased sodium excretion in the perfused kidney was associated with an increase in the clearances of inulin and *para*-aminohippurate ($P < 0.01$) and a decrease in hematocrit of perfusing blood ($P < 0.01$).

Infusion was continued in the donor while recipient was bled 23 ml/kg, with a decrease in mean arterial pressure from 152 to 130 mm Hg. Sodium excretion in perfused kidney decreased from 301 to 142 μEq/min ($P < 0.01$), whereas sodium excretion in donor was unchanged (506 vs. 532 μEq/min; $P > 0.3$). Clearance of inulin by perfused kidney was not significantly affected by bleeding (26 $\pm$SE 2 vs. 25 $\pm$SE 2; $P > 0.2$), but the clearance of *para*-aminohippurate was decreased by bleeding ($P < 0.01$), so that filtration fraction increased.

As the perfused kidney of the recipient dog continued to receive blood from the natriuretic donor dog when the recipient dog was bled, the decrease in sodium excretion that bleeding produced in the perfused kidney was presumably mediated by renal nerves. Thus, an increase in nervous stimuli to the kidney that is not sufficient to decrease glomerular filtration rate can increase the tubular reabsorption of sodium and thereby significantly decrease its excretion. This property of the sympathetic nervous system to affect tubular reabsorption of sodium suggests that an increase in sympathetic activity may constitute an important mechanism for the renal conservation of sodium when intravascular volume is contracted by hemorrhage or other cause.

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INTRODUCTION

Moderate hemorrhage increases sympathetic activity, most likely as a result of the effects of a decrease in effective circulating blood volume on baroreceptors (1). The consequent constriction of arterioles and veins and augmentation of cardiac contraction tend to minimize the decrease in arterial pressure which would occur were it not for an increase in sympathetic activity (2).

If the increase in sympathetic activity does not prevent a decrease in arterial pressure, then a decrease in glomerular filtration occurs and this decrease correlates well with the decrease in arterial pressure (3).

The increase in sympathetic activity also appears to involve the kidneys and to contribute to the decreases in glomerular filtration rate and renal blood flow. Thus, when Dibenzyline, an alpha adrenergic blocking agent, was injected into a renal artery before bleeding, it partially prevented a decrease in glomerular filtration rate and renal blood flow ipsilaterally (4).

A decrease in arterial pressure and an increase in sympathetic activity together provide a potent stimulus to increase the activity of the renin-angiotensin system (5), and, in turn, the production of aldosterone (6, 7). An interaction of these several factors is the probable cause of the decreased renal excretion of sodium that hemorrhage produces.

The present studies were undertaken to evaluate the effect of the sympathetic nervous system per se on renal function in hemorrhage, and to extend the previous observations which suggest that the sympathetic nervous system is part of the mechanism for the renal conservation of sodium (8). In the design of such an experiment, it is necessary to avoid the effects of a decrease in

arterial pressure, and, in so far as possible, to minimize the effects of changes in circulating angiotensin and aldosterone. To accomplish this objective, a donor dog treated with desoxycorticosterone was used to perfuse a kidney of a desoxycorticosterone-treated recipient dog without destruction of the nerve supply to the perfused kidney. Natriuresis was established in the donor dog and in the perfused kidney to permit better characterization of renal nerve discharge as a stimulus to decrease the renal excretion of sodium. The recipient dog was then bled to increase the sympathetic nerve discharge to the perfused kidney that was protected from the other changes that accompany bleeding.

METHODS

For each study, two mongrel dogs weighing 17–28 kg were given a sodium intake of 50 mEq/day for 4 days and desoxycorticosterone, 5 mg i.m., the day before and morning of the study. After both dogs were anesthetized with Pentothal, hydrated with 400–800 ml of normal saline, and anticoagulated with heparin, a femoral artery and vein of the donor dog were connected by polyethelene tubing (PE 280 graduated to PE 400) to the left renal artery and vein of the recipient dog, whose kidney was thus perfused at femoral arterial pressure. Care was taken to preserve the nerve supply to the perfused kidney, except for four studies in which the nerve supply to the perfused kidney was interrupted at the time of cannulation of the renal vessels (experiments 16, 21, 22, and 39). Mean arterial pressure (MAP) was measured in both dogs from catheters in the aorta (9) and urine was collected through ureteral catheters from both kidneys of the recipient dog and one kidney of the donor.

Normal saline containing inulin, *para*-aminohippurate and pitressin, 0.02 U/ml, was infused into both dogs at 1 ml/min by a constant infusion pump. The experimental design is shown schematically in Fig. 1. Clearance measurements were started approximately 1 hr after the operative procedure; three control periods were obtained, then normal saline, 200–1000 ml, was rapidly infused into the donor dog, followed by a continuous infusion of normal saline that contained human albumin, from 2.7 to 3.1 g/100 ml at 15 ml per min, for the remainder of the experiment. The total volume given to the donor dog during an experiment ranged from 2700 to 4000 ml. Blood loss in the recipient dog was replaced by normal saline to prevent an increase in sympathetic activity before experimental hemorrhage. After urine flow from the donor dog and from the perfused kidney of the recipient dog had reached maximal rates, the recipient dog was bled until there was an obvious decrease in urine flow from the perfused innervated kidney. The mean volume of blood shed approximated 2.3% of body weight (mean, 22.7 kg) except in the four experiments in which the perfused kidney was denervated and in these studies it was greater and approximated 3.2% of body weight (mean, 22.8 kg). Each study consisted of 11–16 clearance periods; all clearance periods were 20 min in duration. The clearances of inulin (C_{In}) and *para*-aminohippurate (C_{PAH}) were determined as previously described (9).

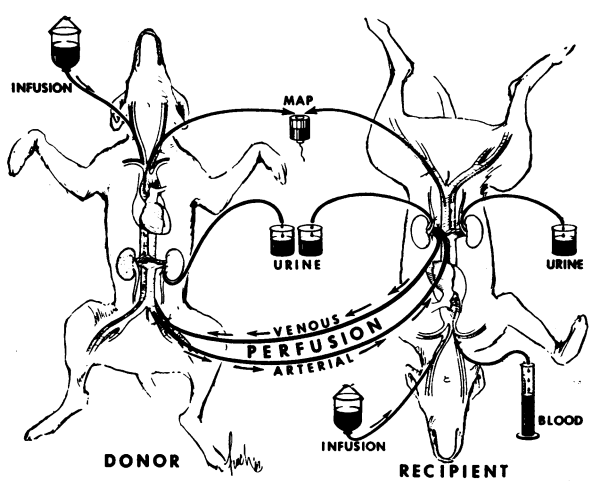

FIGURE 1 Schematic presentation of the experimental procedure. *MAP* = mean arterial pressure.

The values presented are the means of from two to four periods: *a*) immediately before infusion (control), *b*) during infusion when sodium excretion by the perfused kidney was maximal, *c*) during and immediately after hemorrhage (seven experiments plus the four experiments in which the perfused kidney was denervated) and 20–35 min after completion of hemorrhage (experiments 55, 56, 57, 62, and 64). Standard errors of the mean (SE) are presented for C_{In}. The significance of the data was determined by paired analysis.

RESULTS

Fig. 2 shows the results of a study in which natriuresis in a donor dog was maintained by continued infusion while the recipient dog was bled. In the donor, during infusion, sodium excretion increased from 248 to 557 μEq/min with an increase in C_{PAH} and C_{In} but not in MAP. In the recipient dog, sodium excretion in the perfused kidney increased from 73 to 298 μEq/min with an increase in C_{PAH} but not in C_{In}. Sodium excretion in the contralateral kidney was not affected. When the recipient dog was bled, MAP decreased slightly from 145 to 140 mm Hg, and sodium excretion decreased from 143 μEq/min to 87 μEq/min, but C_{PAH} and C_{In} were unchanged. Sodium excretion in the perfused kidney decreased from 298 to 174 μEq/min without a change in C_{PAH} and C_{In}. In the donor dog sodium excretion, MAP, and C_{In} were essentially unchanged, whereas C_{PAH} increased from 141 to 153 ml/min.

The results of 12 such studies are presented in Table I. Infusion in the donor dog increased sodium excretion from a mean value of 112 μEq/min to 532 μEq/min with an increase in mean C_{PAH} from 91 ml/min to 125 ml/min ($P < 0.01$), an increase in mean C_{In} from 33 $\pm$SE 3 to 37 $\pm$SE 3 ($P < 0.05$), and an increase in mean MAP from 154 mm Hg to 169 mm Hg ($P < 0.02$). Mean hematocrit in the donor dog decreased from 46% to 29% ($P < 0.01$).

In the recipient dog, sodium excretion in the perfused kidney increased in response to infusion in the donor dog from a mean value of 60 μEq/min to 301 μEq/min

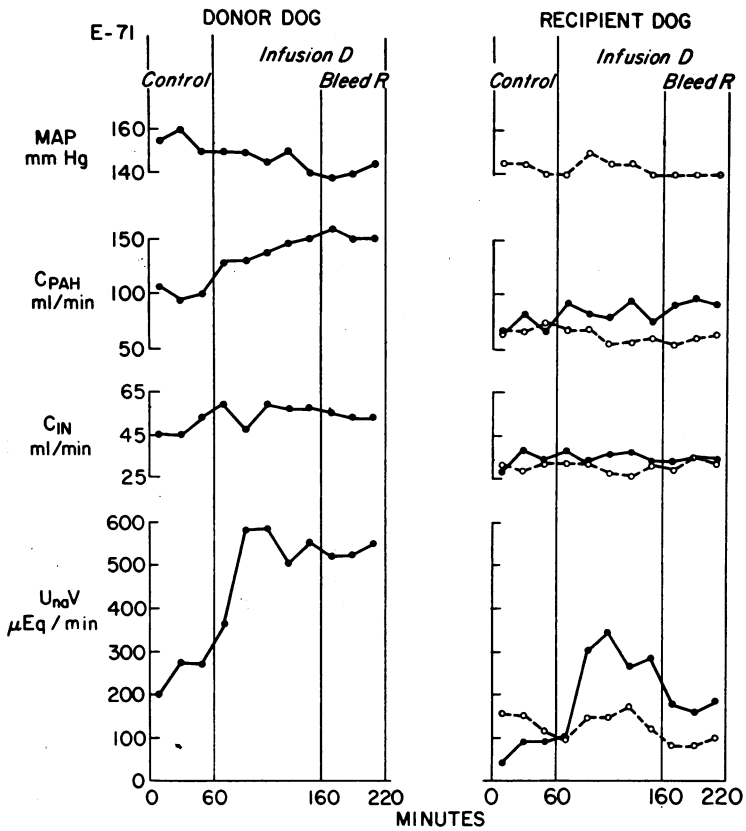

FIGURE 2 Effect of infusion in donor dog (*D*) and of infusion in donor dog together with bleeding of recipient dog (*R*) on *MAP* (mean arterial pressure), C_{PAH} (clearance of *para*-aminohippurate), C_{In} (clearance of inulin) and $U_{Na}V$ (sodium excretion) in the donor dog and in the recipient dog. The solid dots under *recipient dog* denote the perfused kidney. Note that bleeding the recipient dog decreased sodium excretion but did not affect C_{In} in the perfused kidney, and did not change $U_{Na}V$ in donor dog.

($P < 0.01$), with an increase in mean C_{PAH} from 66 ml/min to 91 ml/min ($P < 0.01$) and in mean C_{In} from 23 ±SE 2 to 26 ±SE 2 ($P < 0.01$).

The recipient dog was then bled 23 ml/kg. The results of observations made during and immediately after hemorrhage were similar to the results obtained after a wait of 20–35 min from the end of hemorrhage (experiments 55–57, 62, 64). Mean MAP in the recipient dog decreased with bleeding from 152 to 130 mm Hg ($P < 0.01$). Mean C_{PAH} decreased from 80 ml/min to 69 ml/min ($P < 0.05$), mean C_{In} decreased from 35 ±SE 3 ml/min to 28 ±SE 4 ml/min ($P < 0.01$) and mean sodium excretion decreased from 133 μEq/min to 46 μEq/min ($P < 0.01$). In the perfused kidney, mean sodium excretion decreased from 301 μEq/min to 142 μEq/min ($P < 0.01$) with a decrease in mean C_{PAH} from 91 ml/min to 81 ml/min ($P < 0.01$), but without a change in mean C_{In} (26 ±SE 2 vs. 25 ±SE 2 ml/min) ($P > 0.2$). In the donor dog, mean sodium excretion was sustained (532 vs. 506 μEq/min) as mean C_{PAH}, mean MAP, and mean hematocrit decreased (the latter two variables, significantly, $P < 0.01$), and C_{In} increased ($P < 0.01$).

The results of four studies in which the perfused kidney lacked a normal nerve supply are presented in Table II. Infusion in the donor dog increased sodium excretion in the donor dog from a mean value of 22 μEq/min to 461 μEq/min and in the perfused kidney of the recipient dog from a mean value of 9 μEq/min to 258 μEq/min.

The recipient dog was then bled 32 ml/kg. Mean MAP in the recipient dog decreased with bleeding from 156 to 91 mm Hg. In the two studies in which they were determined, mean C_{PAH} decreased from 70 ml/min to 28 ml/min and mean C_{In} decreased from 34 ml/min to 13 ml/min. Mean sodium excretion decreased from 61 μEq/min to 16 μEq/min. In the perfused kidney, mean sodium

TABLE I

Effects of Infusion in a Donor Dog and of Hemorrhage in the Recipient Dog on Renal Function in the Two Dogs

		Donor dog					Recipient dog						
		Right kidney					Perfused kidney			Contralateral kidney			
Experiment	Regimen	$U_{Na}V$	C_{In}	C_{PAH}	MAP	Hct	$U_{Na}V$	C_{In}	C_{PAH}	$U_{Na}V$	C_{In}	C_{PAH}	MAP
		μEq/min	*ml/min*		*mm Hg*	%	*μEq/min*	*ml/min*		*μEq/min*	*ml/min*		*mm Hg*
55	C*	109	22 ±0.5	59	150	33	24	—	—	7	—	—	142
	I-D‡	724	32 ±0	56	185	21	268	13 ±0	48	145	16 ±0.5	44	150
	H-R§	756	34 ±1.5	53	170	18	80	12 ±0.5	48	52	16 ±0.5	48	152
56	C	44	33 ±2	62	85	39	56	24 ±0.5	60	245	49 ±1	116	157
	I-D	625	44 ±3	111	122	25	343	29 ±0.6	96	154	46 ±1	111	152
	H-R	670	51 ±2	102	122	20	130	28 ±0.5	76	8	32 ±2	84	140
57	C	7	45 ±11	176	178	49	66	26 ±4	80	224	33 ±1	80	170
	I-D	140	39 ±2	174	172	21	392	29 ±1	120	356	39 ±2	80	158
	H-R	259	42 ±0.5	138	162	15	193	30 ±4	119	86	35 ±2	75	125
60	C	66	30 ±2	73	160	45	5	26 ±1	93	16	38 ±1	88	142
	I-D	492	38 ±4.5	129	155	25	180	30 ±2.5	134	98	34 ±1.5	82	136
	H-R	496	45 ±1	132	135	20	73	28 ±1	114	26	26 ±0	68	112
62	C	124	50	104	128	44	6	—	—	56	—	—	138
	I-D	678	50 ±4	96	122	19	156	18 ±3	50	137	42 ±1.5	76	138
	H-R	763	50 ±1.5	100	125	16	88	18 ±0.5	56	16	26 ±0.5	68	120
64	C	9	16 ±2	48	162	43	143	18 ±1.5	40	24	14 ±2.5	43	158
	I-D	393	27 ±2.7	111	182	20	700	22 ±2.7	90	53	32 ±7	66	158
	H-R	352	28 ±2.5	70	185	13	304	22 ±0.5	62	1	—	—	92

C_{In} = mean clearance of inulin ±SE; C_{PAH} = mean clearance of *p*-aminohippurate; MAP = mean arterial pressure; Hct = hematocrit; $U_{Na}V$ = sodium excretion

* C = control

‡ I-D = infusion of normal saline which contained albumin, from 2.7 to 3.1 g/100 ml in the donor dog.

§ H-R = bleeding of recipient dog plus infusion in donor dog.

TABLE I—(*Continued*)

Experiment	Regimen	Donor dog, Right kidney					Recipient dog, Perfused kidney			Recipient dog, Contralateral kidney			
		$U_{Na}V$	C_{In}	C_{PAH}	MAP	Hct	$U_{Na}V$	C_{In}	C_{PAH}	$U_{Na}V$	C_{In}	C_{PAH}	MAP
		μEq/min	*ml/min*		*mm Hg*	%	*μEq/min*	*ml/min*		*μEq/min*	*ml/min*		*mm Hg*
65	C	94	29 ±1	93	162	48	72	17 ±0.3	60	61	27 ±1	78	173
	I-D	352	31 ±1.3	126	195	25	148	20 ±0.3	107	109	25 ±0.7	65	175
	H-R	398	30 ±0.5	111	165	23	82	19 ±4	92	11	17 ±2	38	168
66	C	162	32 ±2.5	72	198	52	94	24 ±1	81	35	40±3	124	178
	I-D	650	24 ±0.5	112	205	44	228	26 ±2	100	30	28 ±8.5	84	150
	H-R	566	30 ±1.5	113	200	28	106	24 ±4	87	35	12 ±9.5	48	85
68	C	130	31 ±3	71	167	50	94	25 ±1	64	158	43 ±1	117	145
	I-D	656	41 ±2	158	158	34	367	33 ±4	107	93	45 ±4	104	145
	H-R	604	45 ±1	164	155	28	198	33 ±1	94	58	37 ±0	90	120
69	C	109	24	67	130	53	59	17	48	228	30	79	150
	I-D	614	29 ±2	143	155	34	238	30 ±0.5	94	91	34 ±0.5	78	155
	H-R	462	34 ±2.5	136	148	27	122	28 ±0.5	88	34	23 ±1	46	148
71	C	248	48 ±3	100	155	48	73	33 ±3	71	140	30 ±1.3	68	143
	I-D	557	55 ±4	141	146	36	298	35 ±1.3	85	143	29 ±2	59	145
	H-R	531	54 ±0.7	153	141	30	174	34 ±0.7	92	87	32 ±2	59	140
74	C	236	35 ±0.7	83	177	43	32	—	—	125	—	—	153
	I-D	497	36 ±1.5	142	228	40	294	22 ±2	60	182	53 ±7	112	156
	H-R	318	40 ±3.5	122	200	29	148	23 ±4	44	140	52 ±0.5	133	162
Mean + SEM	C	112	33 ±3	91	154	46	60	23 ±2	66	110	34 ±4	88	154
	I-D	532	37 ±3	125	169	29	301	26 ±2	91	133	35 ±3	80	152
	H-R	506	40 ±2	116	159	22	142	25 ±2	81	46	28 ±4	69	130
P	C vs. I-D	<0.01	<0.05	<0.01	<0.02	<0.01	<0.01	<0.01	<0.01				
	I-D vs. H-R	>0.3	<0.01	>0.05	<0.01	<0.01	<0.01	>0.2	<0.01	<0.01	<0.01	<0.05	<0.01

TABLE II

Effect of Denervation of Perfused Kidney

Experiment	Regimen	Donor dog, Right kidney $U_{Na}V$	C_{In}	C_{PAH}	MAP	Hct	Recipient dog, Perfused kidney $U_{Na}V$	C_{In}	C_{PAH}	Recipient dog, Contralateral kidney $U_{Na}V$	C_{In}	C_{PAH}	MAP
		μEq/min	*ml/min*		*mm Hg*	*%*	*μEq/min*	*ml/min*		*μEq/min*	*ml/min*		*mm Hg*
16	C*	0			133		11			14			133
	I-D‡	344	20	52	145		376	36	49	109	39	81	132
	H-R§	267	19	46	145		408	33	44	42	22	50	100
21	C	27			162		4			20			183
	I-D	370			185		156			55			180
	H-R	466			178		157			6			82
22	C	16			153		16			50			140
	I-D	482			148		218			55			158
	H-R	450			150		230			13			102
39	C	46	24	46	165	50	5			92	34	54	150
	I-D	648	32	67	156	34	282	40	79	26	29	60	152
	H-R	557	36	69	150	32	277	36	84	4	4	7	80
Mean	C	22			153		9			44			152
	I-D	461	26	60	158		258	38	64	61	34	70	156
	H-R	435	28	58	156		268	34	64	16	13	28	91

Specimens were lost before determination of C_{In} and C_{PAH} for experiments 21 and 22.

* C = control

‡ I-D = infusion of normal saline which contained albumin, from 2.7 to 3.1 g/100 ml in the donor dog.

§ H-R = bleeding of recipient dog plus infusion in donor dog.

C_{In} = mean clearance of inulin; C_{PAH} = mean clearance of *p*-aminohippurate; MAP = mean arterial pressure; Hct = hematocrit; $U_{NA}V$ = sodium excretion.

excretion, mean C_{In}, and mean C_{PAH} showed little change (258 vs. 268 μEq/min, 38 vs. 34 ml/min, and 64 vs. 64 ml/min, respectively). In the donor dog mean sodium excretion, mean C_{In}, mean C_{PAH}, and mean MAP were sustained (461 vs. 435 μEq/min, 26 vs. 28 ml/min, 60 vs. 58 ml/min, and 158 vs. 156 mm Hg, respectively).

DISCUSSION

In 12 studies in which a kidney of a recipient dog with its nerve supply intact was perfused by blood from a donor dog at femoral arterial pressure, the recipient dog showed a significantly lower C_{PAH} ($P < 0.02$) and C_{In} ($P < 0.02$) in the perfused kidney than in the contralateral kidney during the control observations (Table I). Operative manipulation of a kidney can produce as great a decrease in C_{PAH} and C_{In} as that observed in the present studies, and is very likely the reason for the diminished function of the perfused kidney (4). The effect of manipulation on C_{PAH} and C_{In} can be abolished by an injection of Dibenzyline, an alpha adrenergic blocking agent, into the renal artery (4). When the nerve supply to the perfused kidney was interrupted, mean C_{PAH} and C_{In} in the perfused kidney were comparable to those in the contralateral kidney (Table II). Renal denervation at the time of manipulation also appears to prevent alterations in the pattern of renal blood flow that accompany manipulation of the kidney (10). The effects of manipulation therefore probably result from increased renal nerve discharge with vasoconstriction.

Infusion of normal saline, which contained albumin, from 2.7 to 3.1 g/100 ml, in the donor dog produced a natriuresis in the donor dog (532 μEq/min) and in the perfused (301 μEq/min) but not in the contralateral kidney of the recipient dog (Table I). The natriuresis was accompanied by significant increases in MAP, C_{PAH}, and C_{In}, and a significant decrease in hematocrit in the donor dog, and by significant increases in both C_{PAH} and C_{In} in the perfused kidney.

Recent studies suggest that physical factors (increase in mean arterial pressure, decrease in hematocrit, and increase in renal blood flow) (11) and release of a "natriuretic substance" (12) are the principal determinants of the decrease in tubular reabsorption of sodium (13) and of the increased excretion of sodium that occurs in response to expansion of the intravascular vol-

ume with saline or plasma. All of these factors, as well as an increase in glomerular filtration rate, could have mediated the natriuretic response of the donor dog and of the perfused kidney of the recipient dog.

While the infusion was continued in the donor dog, the recipient dog was bled until there was an appreciable decrease in urine flow from the perfused kidney. The result was a 50% decrease in sodium excretion by the perfused kidney from 301 to 142 μEq/min ($P < 0.01$), without a significant change in sodium excretion by the donor dog (532 vs. 506 μEq/min ($P > 0.3$) (Fig. 2, Table I). The decrease in sodium excretion thus occurred despite continued exposure of the perfused kidney to natriuretic stimuli such as hemodilution (14) and, possibly, a circulating "natriuretic substance" (12), which would tend to oppose such a decrease.

Presumably, the sympathetic nerves of the recipient dog which supplied the perfused kidney mediated its response to a blood loss of 23 ml/kg with a decrease in MAP of 14% in the recipient dog. A blood loss of from 10 to 12 ml/kg is sufficient to increase renal resistance and, thus, is probably a sufficient stimulus to increase the rate of discharge of the renal nerves (15). When the sympathetic nerve supply from the recipient dog to the perfused kidney had been interrupted, however, the perfused kidney was unaffected by a blood loss of 32 ml/kg with a decrease in MAP of 42% in the recipient dog.

Whereas the effect of hemorrhage on blood flow was comparable in the innervated perfused and contralateral kidneys (a decrease of 10 ml/min, or 11%, and 11 ml/min, or 14%, respectively), the effect on glomerular filtration rate was considerably greater in the contralateral kidney (a decrease of 7 ml/min, or 20%, as opposed to 1 ml per min) (Table I). Previous studies on the renal response to hemorrhage indicate that the degree of decrease in glomerular filtration rate correlates well with the degree of decrease in arterial pressure (3). Therefore, one would expect the decrease in mean arterial pressure of 22 to 130 mm Hg in the recipient dog to have a greater effect on glomerular filtration rate than the decrease of 10 to 159 mm Hg in the donor dog (Table I). Normally, changes in mean arterial pressure of this magnitude have very little effect on renal blood flow or glomerular filtration rate when vascular tone is normal (16). Thus, the increased renal vascular tone associated with increased sympathetic activity probably accounts for the loss of the normal stability of glomerular filtration rate and its greater dependence upon arterial pressure following hemorrhage.

The decrease in sodium excretion in the perfused innervated kidney when the recipient dog was bled was associated with a significant decrease in mean C_{PAH} ($P < 0.01$), but not in mean C_{In} ($P > 0.2$) in the perfused kidney. These findings suggest that the change in sodium excretion in the perfused kidney which accompanied hemorrhage in the recipient dog resulted from a change in the tubular reabsorption of sodium.

As suggested above, an increase in nervous stimuli to the perfused kidney best explains an increase in sodium reabsorption when it occurs in response to hemorrhage in a dog connected by renal nerves but not by blood supply to that kidney. In this case, the blood was supplied by a donor dog with stable sodium excretion.

An increase in sympathetic nerve discharge could increase the tubular reabsorption of sodium in several ways: first, a decrease in the volume of interstitial fluid around the proximal tubules as a result of an increase in oncotic pressure of the blood in the peritubular capillaries could indirectly lead to an increase in the tubular reabsorption of sodium (17). When the recipient dog was bled, filtration fraction increased from 0.29 to 0.31 in the perfused kidney and this change is compatible with an increase in peritubular capillary oncotic pressure. If, in addition, hemorrhage decreased peritubular capillary hydrostatic pressure, then this change would also tend to decrease the volume of interstitial fluid and to augment the effect of increased capillary oncotic pressure.

Second, an increase in the proportion of total renal glomerular filtrate that traverses juxtamedullary nephrons with long loops and, presumably, with a greater capacity for sodium reabsorption could lead to an increase in the tubular reabsorption of sodium (18). This hypothesis is based on the reports that hemorrhagic hypotension decreased blood flow through the superficial cortex but had little effect on blood flow through the juxtamedullary area (19, 20). More recent studies, however, indicate that hemorrhagic hypotension decreases cortical and medullary blood flow to the same extent and thus do not support the concept of a selective resistance of the juxtamedullary circulation to hemorrhage (21). Conceivably, glomerular filtration rate could increase in the juxtamedullary area relative to the superficial cortical area in response to hemorrhage despite a comparable decrease in blood flow in the two areas. It has recently been suggested that a decrease in the intake of sodium leads to a decrease in glomerular filtration rate in superficial cortical nephrons but an increase in glomerular filtration rate in the juxtamedullary nephrons (22).

Third, an increase in sodium reabsorption could result from a direct effect of the renal nerves or catechols on tubular transport processes. The extent to which any or all of these three mechanisms are operative remains to be established.

Thus, in the present study, a decrease in the volume of extracellular fluid produced by hemorrhage produced a sizable decrease in the renal excretion of sodium with-

out a decrease in glomerular filtration rate, presumably as a result of an increase in the tubular reabsorption of sodium mediated by an increase in sympathetic nervous system activity. In a previous study, a decrease in the volume of extracellular fluid produced by restriction of dietary sodium did not decrease the renal excretion of sodium in a normal fashion despite a decrease in glomerular filtration rate and mean arterial pressure, when sympathetic nervous system activity was blocked, presumably as a result of the inability of the sympathetic nervous system to increase the tubular reabsorption of sodium (8). Together, these two studies provide evidence that the sympathetic nervous system may play an important role in the normal renal conservation of sodium through its ability to increase the tubular reabsorption of sodium.

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