Cardiorenal Reflexes Do Not Attenuate the Renal Effects of Infused Atriopeptin in Conscious Dogs (43477)

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Abstract. **Low-dose infusions of atriopeptin produce only a modest diuresis and natriuresis. However, these infusions also decrease atrial pressures, a change that has been postulated to elicit an antidiuretic and antinatriuretic reflex from cardiac receptors and thereby to attenuate the direct renal effects of atriopeptin. To determine whether the renal effects of intravenously administered atriopeptin might be attenuated by a cardiorenal reflex, we infused α-human atrial natriuretic peptide (α-hANP) into cardiac-denervated and sham-operated (normal) conscious dogs. Following a control period, α-hANP was infused into each dog at 12.5, 25, or 50 ng·kg^{-1}·min^{-1} for 1 hr. Infusion of α-hANP at 50 ng·kg^{-1}·min^{-1} produced similar decreases in left atrial pressure in both normal and cardiac-denervated dogs (peak changes, -1.6 ± 0.8 vs -2.4 ± 0.9 mm Hg, respectively). Increases in urine flow (peak changes, 0.13 ± 0.05 vs 0.20 ± 0.06 ml/min) and sodium excretion (peak changes, 56 ± 22 vs 70 ± 11 μEq/min) also were not different between groups. The lower doses of α-hANP also elicited renal and hemodynamic responses in the cardiac-denervated dogs that did not differ significantly from those in the normal dogs. These data indicate that the diuresis and natriuresis elicited by intravenously administered α-hANP are not attenuated by a cardiorenal reflex in conscious dogs.** [P.S.E.B.M. 1992, Vol 201]

Low-dose infusions of atriopeptin produce relatively modest increases in urine flow and sodium excretion (1–7). We have reported, for example, that a 12-fold increase in circulating atriopeptin produces only a doubling of urine flow and sodium excretion in conscious dogs (1). Low-dose infusions of atriopeptin also decrease atrial pressures (1, 2, 5, 8–10). It has been suggested that the decrease in atrial pressures may elicit a reflex from cardiac receptors that opposes the renal excretory effects of atriopeptin (5), and may account for the modest diuretic effect of exogenously administered atriopeptin.

It is well known that a reflex from atrial receptors can alter renal function under experimental conditions. For example, Henry and Pearce (10) demonstrated nearly 40 years ago that urine flow increases when the left atrium is distended by a balloon. Later, it was demonstrated that left atrial distension in the conscious dog increases sodium excretion as well as urine flow (11–13). The diuretic and natriuretic responses elicited by atrial stretch depend upon cardiac neural pathways; atrial stretch does not alter urine flow or sodium excretion in dogs with chronically denervated hearts (11, 14, 15). More recently, studies have indicated that the renal response to left atrial distension is not dependent upon the release of atriopeptin (14, 16).

A similar neural mechanism may contribute to the decrease in urine flow and sodium excretion observed when cardiac transmural pressure is reduced. Evidence consistent with this notion is that urine flow and sodium excretion decrease when cardiac transmural pressure is decreased by either cardiac tamponade (17) or positive end-expiratory pressure ventilation (18, 19). Although cardiac tamponade and positive end-expiratory pressure ventilation doubtless alter systemic hemodynamics, these studies do provide evidence to suggest that a neural component is involved in the antidiuresis and antinatriuresis elicited by these maneuvers.

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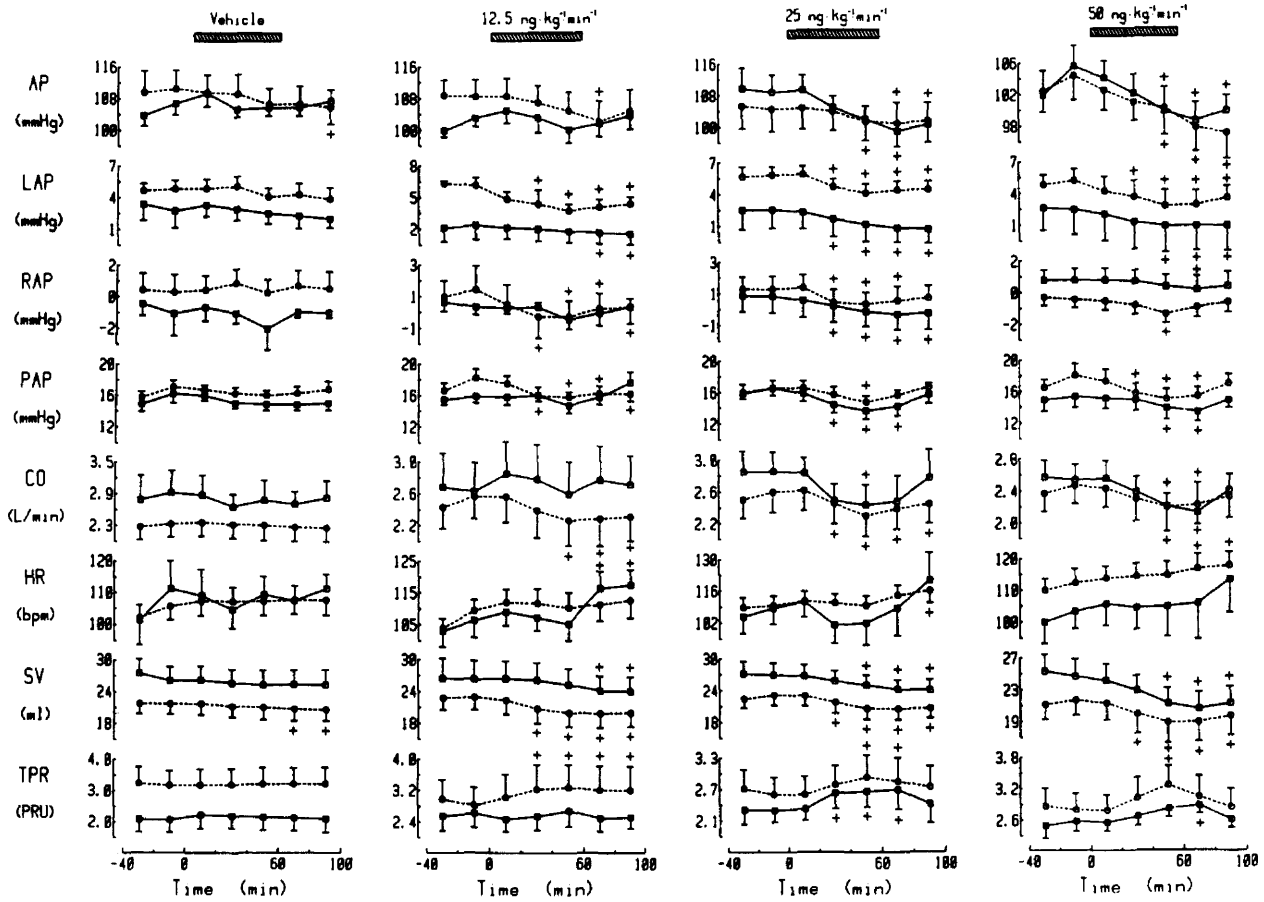

Figure 1. Hemodynamic variables measured during α-hANP infusion for 60 min at doses of 0 (vehicle), 12.5, 25, and 50 ng·kg^{-1}·min^{-1} in normal (solid lines) and cardiac-denervated (broken lines) conscious dogs. Horizontal hatched bars indicate infusion periods. Abbreviations used in figure: AP, mean arterial pressure; LAP, left atrial pressure; RAP, right atrial pressure; PAP, pulmonary arterial pressure; CO, cardiac output; TPR, total peripheral resistance; HR, heart rate; SV, stroke volume. +, $P < 0.05$ versus mean data from −20 to 0 min within each group.

To determine whether the decrease in atrial pressures that is elicited by infusion of atriopeptin might reflexly attenuate the direct diuretic and natriuretic action of atriopeptin, we compared the renal response to low-dose constant infusions of atriopeptin in normal dogs with the response to identical infusions in dogs in which cardiac reflexes had been abolished by chronic cardiac denervation.

Materials and Methods

Surgical Procedures and Animal Care. Eighteen female mongrel dogs were divided randomly into either a sham-operated ([normal] $n = 8$) or cardiac-denervated ($n = 10$) group. Dogs were anesthetized with sodium pentobarbital (25 mg/kg, iv, with supplements given as needed), and a thoracotomy was performed aseptically through the left fourth intercostal space. Polyethylene catheters were placed in the descending aorta, the pulmonary artery, and the right and left atria. Also, an ultrasonic transit-time flow probe (Transonics System, Inc., Ithaca, NY) was placed around the ascending aorta to measure cardiac output (minus coronary blood flow). Cardiac-denervated dogs were prepared by the intrapericardial denervation technique of Randall *et al.* (20) as modified by Fater *et al.* (11) in our laboratory. Briefly, all visible nerves within the pericardium were cut and the adventitia surrounding the great vessels and pulmonary veins was stripped. All catheters and the flow probe cable were tunneled subcutaneously and brought out through the skin in the back. A flexible infant-feeding tube was placed in the chest for reduction of the pneumothorax immediately after surgery and for daily removal of chest fluid for several days after surgery. Morphine (15 mg, im) was administered postoperatively to relieve pain and penicillin (500,000 units, im) was given daily for 3 days after surgery. The dogs were allowed at least 2 weeks to recover from surgery before experiments were conducted.

Catheters were flushed two to three times per week with a solution of sodium heparin (1000 units/ml) to prevent clotting. The dogs were fed every afternoon with a mixture of canned and dry food that provided a total of 65 mEq of sodium per day. Free access to water was provided at all times.

Table I. Hemodynamic Responses to α-hANP Infusion[a]

	LAP (mm Hg)		MAP (mm Hg)		HR (bpm)		Co (liters/min)		SV (ml)		TPR (PRU)	
	C	I	C	I	C	I	C	I	C	I	C	I
Vehicle												
N	2.7 ± 1.6	2.5 ± 1.0	107 ± 3	106 ± 2	111 ± 9	109 ± 6	2.9 ± 0.4	2.8 ± 0.4	26 ± 3	25 ± 3	2.1 ± 0.4	2.2 ± 0.4
CD	4.8 ± 0.8	4.1 ± 0.9	110 ± 5	107 ± 4	106 ± 4	107 ± 5	2.3 ± 0.3	2.3 ± 0.3	22 ± 2	21 ± 2	3.2 ± 0.5	3.2 ± 0.5
α-hANP 12.5 ng·kg^{-1}·min^{-1}												
N	2.4 ± 1.4	1.7 ± 1.1	103 ± 2	100 ± 3	106 ± 5	105 ± 5	2.6 ± 0.4	2.6 ± 0.4	26 ± 3	25 ± 3	2.6 ± 0.4	2.7 ± 0.4
CD	6.2 ± 0.7	3.7 ± 0.6[b]	108 ± 4	105 ± 5	109 ± 3	110 ± 5	2.6 ± 0.3	2.3 ± 0.3[b]	23 ± 2	20 ± 3[b]	2.8 ± 0.5	3.3 ± 0.6[b]
α-hANP 25 ng·kg^{-1}·min^{-1}												
N	2.6 ± 1.7	1.2 ± 1.6[b]	109 ± 4	102 ± 3	109 ± 7	102 ± 10	2.9 ± 0.3	2.4 ± 0.3[b]	27 ± 2	25 ± 2[b]	2.3 ± 0.2	2.7 ± 0.3[b]
CD	5.9 ± 0.8	4.1 ± 0.9[b]	105 ± 6	101 ± 5[b]	110 ± 4	110 ± 4	2.6 ± 0.3	2.3 ± 0.3[b]	23 ± 2	21 ± 2[b]	2.6 ± 0.3	2.9 ± 0.4
α-hANP 50 ng·kg^{-1}·min^{-1}												
N	2.4 ± 2.4	0.8 ± 2.5[b]	106 ± 3	100 ± 3[b]	103 ± 5	105 ± 9	2.5 ± 0.2	2.2 ± 0.2[b]	25 ± 2	21 ± 2[b]	2.6 ± 0.2	2.8 ± 0.2
CD	5.1 ± 1.1	2.7 ± 1.5[b]	104 ± 6	100 ± 3[b]	112 ± 5	115 ± 4	2.5 ± 0.2	2.2 ± 0.3[b]	22 ± 2	19 ± 3[b]	2.8 ± 0.3	3.3 ± 0.5[b]

[a] Values are mean ± SE. Control data (C) were obtained during the 20 min before α-hANP or vehicle infusion. Infusion data (I) were obtained during the final 20 min of the 1-hr infusion period. Abbreviations used in table: N, normal dogs; CD, cardiac-denervated dogs; LAP, left atrial pressure; MAP, mean arterial pressure; HR, heart rate; CO, cardiac output; SV, stroke volume; TPR, total peripheral resistance; PRU, peripheral resistance units.

[b] $P < 0.05$ versus control within group.

Tests for Cardiac Denervation. Electrical stimulation of the ansae subclavii and the thoracic vagi during the surgery, but before denervation, produced the expected increases and decreases in heart rate, respectively. Completeness of cardiac denervation was verified by the absence of changes in R-R interval on the electrocardiogram in response to electrical stimulation of these same nerves immediately following the denervation procedure.

Approximately 1 week after the surgery, pharmacological tests for cardiac denervation were performed. Methoxamine (50 μg/kg) and nitroglycerin (24 μg/kg) were injected intravenously to raise and lower blood pressure, respectively. The absence of changes in heart rate (±6 bpm) within the first 18 sec after administration of these drugs confirmed that efferent nerves to the heart were effectively denervated. In addition, veratridine (25 μg) was injected into the left atrium; the absence of any changes in arterial blood pressure (±5 mm Hg) provided evidence that the afferent neural pathway responsible for the Bezold-Jarisch reflex had been effectively eliminated. Previous studies from our laboratory have shown that this cardiac denervation technique also interrupts the cardiac afferent nerves responsible for the diuresis and natriuresis that normally occurs during left atrial distension in normal dogs (11, 14). Previous work from our laboratory also indicates that dogs undergoing cardiac-denervation remain denervated for at least 4 weeks after surgery (11). All experiments in the present study were performed within 4 weeks from the date of surgery.

Experimental Prococol. On the day of the experiment, a self-retaining bladder catheter was inserted. The dogs were placed in a Pavlov-type sling in which they rested quietly throughout the experiment. After two 20-min control periods, α-human atrial natriuretic peptide [α-hANP] Peninsula Laboratories, Belmont, CA) was administered intravenously at doses of 0 (vehicle), 12.5, 25, or 50 ng·kg^{-1}·min^{-1} for 1 hr; this was followed by two 20-min recovery periods. The appropriate amount of α-hANP was dissolved in 15 ml of 5% dextrose in water and infused into a temporary leg vein catheter with an infusion pump (Harvard Apparatus, South Natick, MA).

Vascular catheters were connected to Gould 23xL pressure transducers and blood pressures were monitored continuously by an oscillographic recorder. The signals were converted to digital format at 100 samples/sec and stored as 1-min averages for later analysis (PDP-11/34; Digital Equipment Corp., Maynard, MA).

Urine samples were collected at 20-min intervals. Arterial blood samples were collected 5 min before the infusion was started and 25 min after beginning the infusion. Blood samples were replaced with an equal volume of isoncotic dextran in isotonic saline.

Analytical Procedures. Urine sodium and potas-

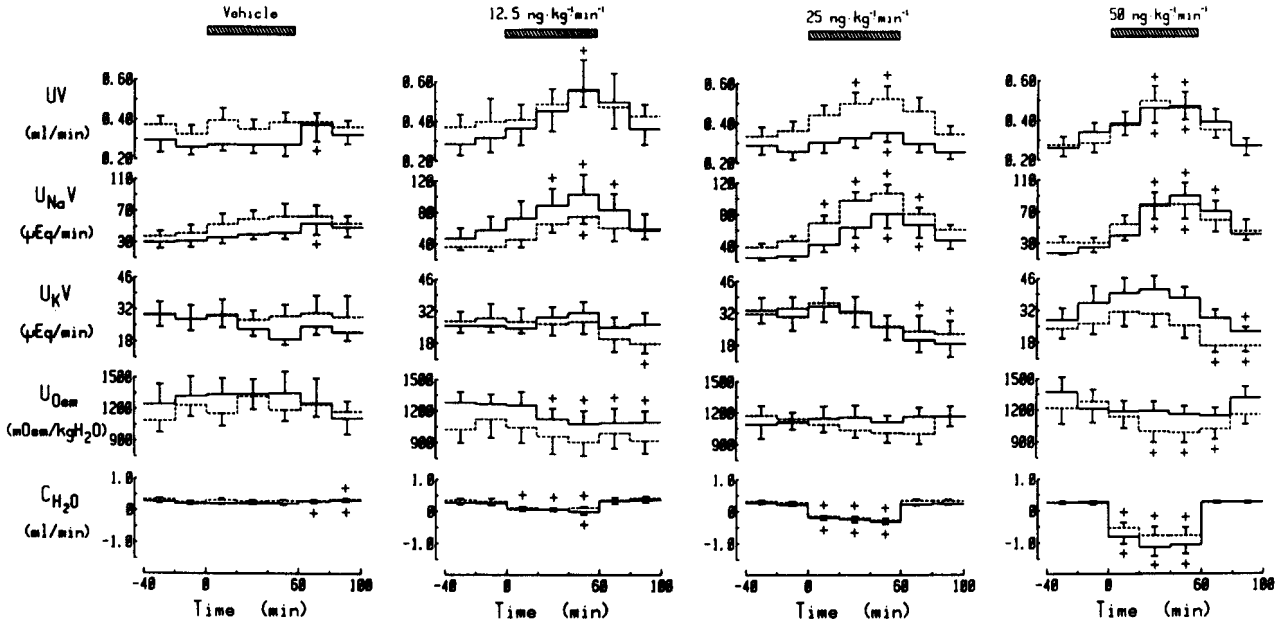

Figure 2. Renal variables measured during α-hANP infusion for 60 min at doses of 0 (vehicle), 12.5, 25, and 50 ng·kg^{-1}·min^{-1} in normal (solid lines) and cardiac-denervated (broken lines) conscious dogs. Horizontal hatched bars indicate infusion periods. Abbreviations used in this figure UV, urine flow; $U_{Na}V$, sodium excretion; U_KV, potassium excretion; U_{Osm}, urinary osmolality; C_{H2O}, free water clearance. +, $P < 0.05$ versus mean data from −20 to 0 min within each group.

Table II. Renal Responses to α-hANP Infusion[a]

	UV (ml/min)		$U_{Na}V$ (μEq/min)		U_KV (μEq/min)	
	C	I	C	I	C	I
Vehicle						
N	0.26 ± 0.04	0.27 ± 0.06	31 ± 8	40 ± 8	27 ± 5	18 ± 3
CD	0.32 ± 0.05	0.38 ± 0.05	41 ± 11	62 ± 16	28 ± 6	28 ± 5
α-hANP 12.5 ng·kg^{-1}·min^{-1}						
N	0.32 ± 0.07	0.56 ± 0.15[b]	57 ± 18	102 ± 25[b]	25 ± 3	31 ± 5
CD	0.40 ± 0.12	0.55 ± 0.08	36 ± 5	74 ± 9[b]	29 ± 7	27 ± 5
α-hANP 25 ng·kg^{-1}·min^{-1}						
N	0.25 ± 0.04	0.35 ± 0.05[b]	27 ± 5	81 ± 19[b]	30 ± 6	26 ± 6
CD	0.36 ± 0.05	0.52 ± 0.07[b]	46 ± 7	106 ± 12[b]	34 ± 5	26 ± 5
α-hANP 50 ng·kg^{-1}·min^{-1}						
N	0.34 ± 0.05	0.47 ± 0.07[b]	25 ± 6	91 ± 16[b]	35 ± 7	37 ± 5
CD	0.29 ± 0.05	0.46 ± 0.06[b]	31 ± 7	79 ± 18[b]	26 ± 5	26 ± 6

[a] Values are mean ± SE. Control data (C) were obtained during the 20 min before α-hANP or vehicle infusion. Infusion data (I) were obtained during the final 20 min of the 1-hr infusion period. Abbreviations used in table: N, normal dogs; CD, cardiac-denervated dogs; UV, urine flow; $U_{Na}V$, urinary sodium excretion; U_KV, urinary potassium excretion.
[b] $P < 0.05$ versus control within group.

sium concentrations were measured by flame photometry (model 943; Instrumentation Laboratories, Lexington, MA). Urine osmolality was measured by freezing point depression (model 3MO; Advanced Instruments, Needham Heights, MA). Atriopeptin in plasma was measured by radioimmunoassay, as described previously (21). Briefly, arterial blood samples were transferred immediately to chilled tubes containing EDTA and kept on ice until processing. Plasma was separated by centrifugation at 4°C and stored at −20°C until assayed. Plasma was extracted with Sep-Pak C_{18} cartridges (Waters Associates, Milford, MA) and analyzed by radioimmunoassay using antiserum from Peninsula Laboratories and ^{125}I-labeled α-hANP from Amersham (Arlington Heights, IL). Arginine vasopressin was extracted from plasma with Sep-Pak C_{18} cartridges and measured by radioimmunoassay (22). Plasma renin activity was determined by the method of Haber *et al.* (23) using reagents purchased as a kit from Incstar clinical assays (Stillwater, MN). Plasma aldosterone was measured with a solid-phase radioimmunoassay kit (Diagnostic Products, Los Angeles, CA).

Statistical Analyses. Hemodynamic and renal data were averaged over consecutive 20-min periods.

Table III. Hormonal Responses to α-hANP Infusion[a]

	irAP (pg/ml)		PRA (ngAI·ml^{-1}·hr^{-1})		ALDO (ng/dl)		AVP (pg/ml)	
	C	I	C	I	C	I	C	I
Vehicle								
N	62 ± 8	58 ± 7	1.2 ± 0.1	1.8 ± 0.3[b]	2.0 ± 0.6	2.8 ± 0.7	4.8 ± 2.4	4.7 ± 2.0
CD	81 ± 10	70 ± 5[b]	0.9 ± 0.2	1.2 ± 0.2	6.0 ± 3.3	6.9 ± 3.2	3.0 ± 1.5	4.1 ± 1.8
α-hANP 12.5 ng·kg^{-1}·min^{-1}								
N	61 ± 7	282 ± 36[b]	1.1 ± 0.2	1.6 ± 0.6	2.4 ± 0.9	3.0 ± 1.2	3.1 ± 5.9	5.9 ± 1.7
CD	68 ± 4	238 ± 33[b]	1.4 ± 0.2	1.1 ± 0.3	3.9 ± 2.0	2.3 ± 1.0	3.7 ± 2.5	4.8 ± 1.8
α-hANP 25 ng·kg^{-1}·min^{-1}								
N	55 ± 4	567 ± 62[b]	1.4 ± 0.5	0.9 ± 0.2	2.0 ± 0.6	1.1 ± 0.1	2.6 ± 3.9	3.9 ± 0.8
CD	77 ± 8	463 ± 25[b]	1.2 ± 0.3	1.0 ± 0.4	3.0 ± 2.0	2.0 ± 1.0	3.4 ± 2.3	3.8 ± 2.1
α-hANP 50 ng·kg^{-1}·min^{-1}								
N	57 ± 5	1087 ± 170[b]	1.4 ± 0.3	0.9 ± 0.2[b]	5.7 ± 2.2	2.6 ± 1.2	6.6 ± 1.8	13.4 ± 3.4
CD	68 ± 5	961 ± 104[b]	1.5 ± 0.3	1.2 ± 0.4	8.8 ± 5.4	6.7 ± 4.2	5.1 ± 2.1	4.5 ± 1.7

[a] Values are mean ± SE. Blood samples were collected 5 min before α-hANP or vehicle infusion (C) and 25 min after the infusion began (I). Abbreviations used in table: N, normal dogs; CD, cardiac-denervated dogs; irAP, immunoreactive atriopeptin; PRA, plasma renin activity; ALDO, aldosterone; AVP, arginine vasopressin. irAP and PRA were measured in all dogs. ALDO and AVP were measured in four normal dogs and in three CD dogs.
[b] $P < 0.05$ versus control within group.

Data were analyzed by two-way analysis of variance for repeated measures. Within groups, Dunnett's test was used to determine which means differed significantly from the control means. A series of completely randomized F tests was used to determine whether differences existed between the two groups during each experimental period (24). All data are expressed as mean ± SE. *P*-values of less than 0.05 were considered to be statistically significant.

Results

Hemodynamic Results. Infusion of α-hANP at 50 ng·kg^{-1}·min^{-1} decreased arterial pressure, left atrial pressure, right atrial pressure, pulmonary artery pressure, cardiac output, and stroke volume in both normal and cardiac-denervated dogs; total peripheral resistance increased in both groups (Fig. 1 and Table I). Heart rate tended to increase in both groups, particularly after the infusion was stopped. Similar trends in the hemodynamic response to α-hANP infusion were observed at the lower infusion rates. Infusion of α-hANP at each rate produced hemodynamic responses in the cardiac-denervated dogs that did not differ significantly from responses in the normal dogs. Hemodynamics were quite stable during vehicle infusion; only isolated, minor decreases in arterial pressure and stroke volume were detected in the cardiac-denervated dogs at the end of the experiment.

Renal Results. Infusion of α-hANP at each rate increased urine flow and sodium excretion and decreased free water clearance in both groups of dogs (Fig. 2 and Table II). Changes in potassium excretion and urine osmolality were variable at the different infusion rates. No significant differences in renal responses were detected between groups. Renal function remained quite constant during the vehicle infusion experiments; only isolated changes in urine flow and sodium excretion in the normal dogs and slight increases in free water clearance near the end of the experiment in both groups were detected.

Hormone Levels. Basal plasma levels of immunoreactive atriopeptin averaged between 55 and 81 pg/ml and were not significantly different between the normal and cardiac-denervated dogs (Table III). Infusion of α-hANP at 12.5, 25, and 50 ng·kg^{-1}·min^{-1} increased plasma levels of immunoreactive atriopeptin approximately 4-, 8-, and 17-fold, respectively. Plasma renin activity increased significantly in the normal dogs during vehicle infusion. Plasma renin activity decreased significantly during infusion of α-hANP at 50 ng·kg^{-1}·min^{-1} in the normal dogs only, but was unaltered at the lower doses in all dogs. Plasma levels of aldosterone and vasopressin levels were not altered significantly during infusion of vehicle or α-hANP at any rate. No significant differences in plasma levels of any hormone measured were detected between normal and cardiac-denervated dogs during the control period or during infusion of α-hANP at each rate of infusion.

Discussion

The increase in urine flow and sodium excretion elicited by intravenously administered atriopeptin in cardiac-denervated dogs in this study was statistically indistinguishable from the renal responses elicited in normal dogs. Accordingly, these results do not support the notion that cardiorenal reflexes are capable of attenuating the diuretic and natriuretic effects of exogenously administered atriopeptin in conscious dogs. Administration of atriopeptin produced only modest increases in urine flow and sodium excretion, regardless

of whether cardiorenal reflexes were present or not. We have not, however, excluded the possibility that the combined increases in atrial pressure and circulating atriopeptin that probably occur in some physiological situations may act synergistically to enhance urine flow and sodium excretion.

Even though earlier experiments have illustrated that changes in atrial pressure are capable of eliciting reflex changes in urine flow and sodium excretion (11, 14), the results from the present study suggest that cardiorenal reflexes do not alter the renal response to an infusion of atriopeptin in conscious dogs. It seems quite possible that the decreases in atrial pressure were sufficient to alter cardiorenal reflexes (9), but no renal effect was detected in the present experiments. It is conceivable, though, that lower levels of atrial pressure than those achieved in the present study may be required to elicit an antinatriuretic cardiorenal reflex. However, further decreases in atrial pressure would require administration of greater doses of atriopeptin, which would increase plasma levels much higher than would be expected to occur in even pathophysiological situations.

The basal hemodynamic, renal, and hormonal status of the two groups of dogs were very similar. This is consistent with previous data from our laboratory (21) and others (25) that failed to reveal any significant differences between normal and cardiac-denervated dogs under basal conditions. Furthermore, the lack of a difference in the renal response between groups in the present study cannot be explained by differences in the hemodynamic and hormonal responses to atriopeptin infusion; hemodynamic and hormonal changes elicited by infusion of atriopeptin were similar in normal and cardiac-denervated dogs.

The renal response to low doses of atriopeptin was quite modest. For example, infusion of atriopeptin at 12.5 $ng \cdot kg^{-1} \cdot min^{-1}$ increased sodium excretion in the normal and cardiac-denervated dogs from 57 ± 18 to 102 ± 25 μEq/min and from 36 ± 5 to 74 ± 9 μEq/min, respectively. The magnitude of these changes is comparable to the changes in sodium excretion reported by Hisa *et al.* (25) in response to intrarenal infusion of atriopeptin at 10 $ng \cdot kg^{-1} \cdot min^{-1}$ (from 29 ± 16 to 70 ± 39 μEq/min). The similarity in these results provides further evidence to support the conclusion that cardiorenal reflexes do not alter the renal response to intravenously administered atriopeptin.

The renal response to low doses of atriopeptin is quite modest and does not exhibit a tight dose-response relationship. For example, infusion of α-hANP into normal dogs at 25 $ng \cdot kg^{-1} \cdot min^{-1}$ produced changes in urine flow and sodium excretion that were less than the changes elicited by infusions at 12.5 and 50 $ng \cdot kg^{-1} \cdot min^{-1}$; similar responses were observed by Bie *et al.* (1). This variability might have hindered the detection of other possible influences, such as cardiorenal reflexes, on renal function. Differences in the reflex activation of the sympathetic nervous system between groups, including the renal sympathetic efferent nerves, in response to atriopeptin-induced reductions in mean arterial pressure may also have contributed to the variability of the renal response. For example, infusion of atriopeptin at 25 and 50 $ng \cdot kg^{-1} \cdot min^{-1}$ significantly altered systemic blood pressure, a change that might result in activation of responses that would oppose the renal action of atriopeptin. Although it is possible that the magnitude of these opposing responses might be different in the two groups, atriopeptin infusion at 12.5 $ng \cdot kg^{-1} \cdot min^{-1}$, a dose that did not alter systemic hemodynamics, produced significant changes in renal function in both groups of dogs that were not different between groups.

In spite of intense investigation, it is still not established that circulating atriopeptin exerts an appreciable influence on the physiological regulation of sodium excretion. Evidence for and against this view was summarized in a debate between Goetz (26) and Blaine (27). Emerging evidence does suggest, however, that a more recently discovered member of the atriopeptin family, urodilatin, may be more important in regulating sodium excretion than atriopeptin. Urodilatin was discovered in human urine and appears to be synthesized in the kidney (28). It is identical to α-hANP, except that it contains four additional residues at the N-terminal. Urodilatin is reportedly more natriuretic than α-hANP on a molar basis when infused into dogs (29, 30), and it is resistent to a renal enzyme that degrades atriopeptin (31). Moreover, the excretion of urodilatin correlates better with renal sodium excretion than does atriopeptin in conscious dogs (32), and in normal human subjects (33). These and other data have led to the hypothesis that the renal natriuretic peptide (perhaps urodilatin) participates in the intrarenal regulation of sodium transport and that atriopeptin is primarily a regulator of the cardiovascular system (34).

In conclusion, the present results indicate that low-dose infusions of atriopeptin are capable of eliciting only a modest diuresis and natriuresis, even when administered to dogs with complete cardiac denervation. Accordingly, this study indicates that cardiorenal reflexes do not attenuate the direct diuretic and natriuretic effects of exogenously administered atriopeptin in conscious dogs.

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