Renal Mechanisms for Suppression of Renin Secretion by Atrial Natriuretic Factor

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SUMMARY The effects of synthetic atrial natriuretic factor on renin secretion were examined in anesthetized dogs with either a single filtering kidney or a single denervated nonfiltering kidney. In dogs with a single filtering kidney (Series 1, n = 6), a priming dose of atrial natriuretic factor (2 µg/kg, i.v.) followed by sustained intravenous infusions at doses of 200 and 400 ng/kg/min for 20 minutes each produced striking decrements (p < 0.05) in renin secretion, from 1083 ± 322 to 205 ± 120 and 286 ± 168 ng of angiotensin I per minute. This fall in renin secretion was associated with significant increases (p < 0.05) in creatinine clearance, urine flow, sodium excretion, and the filtered load of sodium. Renal blood flow increased only transiently. In dogs with a single denervated nonfiltering kidney (Series 2, n = 6), infusion of atrial natriuretic factor at these doses also produced marked inhibition (p < 0.05) of renin secretion, from 311 ± 98 to 72 ± 22 and 91 ± 37 ng of angiotensin I per minute. Renal blood flow remained significantly elevated (p < 0.05) throughout the infusion, in contrast to renal blood flow in Series I. Similar results were obtained in a third series of dogs (n = 6) with a single denervated nonfiltering kidney, during sustained intrarenal arterial infusions of atrial natriuretic factor. These results suggest that an increase in the sodium load delivered to the macula densa is not essential for the inhibition of renin secretion by atrial natriuretic factor. We conclude that suppression of renin secretion by atrial natriuretic factor is mediated through its interactions with the two intrarenal receptor mechanisms, the renal vascular receptor and the macula densa. It is also possible that atrial natriuretic factor has a direct inhibitory action on the juxtaglomerular cells.

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KEY WORDS • anesthetized dogs • glomerular filtration • macula densa • renal vascular receptor • natriuresis • filtered sodium load

CARDIAC atrial tissue contains a family of structurally related polypeptides referred to as atriopeptins1 or as atrial natriuretic factor (ANF).2,3 Various laboratories have purified and determined the amino acid sequence of several atrial peptides, and synthetic compounds with these structures have the same biological properties as the natural peptides.4-8 Natriuresis and diuresis are the most thoroughly characterized biological effects of the ANF peptides.9 These effects may be partially related to a direct inhibition of tubular sodium transport10-13 and to increments in the glomerular filtration rate.10,11,14-18 ANF peptides are reported to be selective renal vasodilators and to increase renal blood flow in dogs.19,20 They increase in renal blood flow induced by continuous infu-
sustained intravenous infusion of the peptide at the rate of 200 ng/kg/min for the first 20-minute clearance period and at the rate of 400 ng/kg/min for the next clearance period. The infusion of ANF was followed by two 20-minute recovery periods. During the last 4 minutes of each period, renal venous and systemic arterial blood samples were collected for measurements of plasma renin activity and hematocrit. MAP and RBF were recorded continuously. The synthetic ANF peptide used in all the experiments in this study corresponds to the 28-amino acid peptide structure of the natural rat ANF that has been described by Flynn et al. 6

Methods

Female mongrel dogs (n = 18) with body weights between 16 and 25 kg were used in this study. The dogs were housed in individual metabolism cages and maintained on a diet that provided approximately 60 mEq of sodium and 55 mEq of potassium daily for at least 8 days before the study and until sodium excretion approximated sodium intake. Water was available ad libitum.

All experiments were performed while the dogs were in the postabsorptive state. On the morning of the experiment, the dogs were anesthetized with sodium pentobarbital (30 mg/kg, i.v.), and supplemental small doses of the drug were administered intravenously as needed to maintain a surgical plane of anesthesia. Polyethylene catheters (8F) were inserted into the femoral vessels, and their tips advanced into the inferior vena cava and abdominal aorta. The arterial catheter was connected by a Statham P23Db strain gauge pressure transducer (Oxnard, CA, USA) to a Hewlett Packard 7702B recorder (St. Louis, MO, USA), to monitor mean arterial pressure (MAP) and heart rate. The femoral vein catheter was used for infusion of solutions and for the replacement of blood. Both kidneys were exposed through retroperitoneal flank incisions, and a unilateral nephrectomy was performed to remove any influence of this kidney on renin secretion. The contralateral renal artery was fitted with an electromagnetic flow probe connected to a Model 501 Carolina Electronics flowmeter (Burlington, NC, USA) for determination of renal blood flow (RBF). A 22-gauge curved needle attached to polyethylene tubing was inserted into the renal vein to obtain renal venous samples. A 60-minute equilibration period followed the surgical preparations and preceded the experiments. In all experiments, blood withdrawn for sampling was replaced with an equal volume of fresh donor blood from a normal dog.

Series 1: Intravenous Infusion of Atrial Natriuretic Factor in Dogs with a Single Filtering Kidney

A priming bolus (1 ml/kg) of an isotonic solution containing 3.6% (wt/vol) creatinine was given to each dog (n = 6), and a constant infusion at a rate of 0.6 ml/min was maintained throughout the experiment for the determination of creatinine clearance. A ureteral catheter was positioned near the renal pelvis for quantitative collection of urine. Systemic arterial blood samples were obtained at the midpoint of each clearance period for the determination of plasma creatinine and electrolyte concentrations. Control values for renal clearance were determined during three 20-minute periods. A priming dose of 2 μg/kg of synthetic rat ANF peptide (Peninsula Laboratories, Belmont, CA, USA) was given intravenously as a bolus, followed by a sustained intravenous infusion of the peptide at the rate of 200 ng/kg/min for the first 20-minute clearance period and at the rate of 400 ng/kg/min for the next clearance period. The infusion of ANF was followed by two 20-minute recovery periods. During the last 4 minutes of each period, renal venous and systemic arterial blood samples were collected for measurement of plasma renin activity and hematocrit. MAP and RBF were recorded continuously. The synthetic ANF peptide used in all the experiments in this study corresponds to the 28-amino acid peptide structure of the natural rat ANF that has been described by Flynn et al. 6

Series 2: Intravenous Infusion of Atrial Natriuretic Factor in Dogs with a Single Denervated Nonfiltering Kidney

Four days before the ANF infusion, each dog (n = 6) underwent surgery to produce a denervated nonfiltering kidney, as described by Blaine and Davis. 12, 13 Briefly, under sodium pentobarbital anesthesia (30 mg/kg, i.v.) one of the kidneys was exposed through a retroperitoneal flank incision. The renal artery was totally occluded for 2 hours with a serrefine clamp. After restoration of the RBF, the ureter was ligated and sectioned, and the kidney was denervated by stripping all visible renal nerves and painting the renal vessels with 5% phenol. This experimental preparation remains responsive to many physiological stimuli for renin secretion but renders nonfunctional the macula densa and the renal nerve mechanisms for the control of renin release. On the day of the experiment the animal was anesthetized as described in Series 1, the contralateral filtering kidney was removed, and an adjustable clamp was positioned around the suprarenal aorta. After three 20-minute control periods, an ANF infusion protocol identical to that described for Series 1 was performed for two 20-minute experimental periods, followed by two 20-minute recovery periods. After the second recovery period, the renal perfusion pressure was reduced by approximately 50% with the suprarenal aortic clamp for one additional 20-minute period to stimulate renin release. This was done to determine the functional status of the renal vascular receptor mechanism for renin release. At the end of each experiment the kidney was decapsulated, and lissamine green dye was injected to verify that the kidney was not filtering the dye into the tubular system. 22, 23

Series 3: Intravenous Infusion of Atrial Natriuretic Factor in Dogs with a Single Denervated Nonfiltering Kidney

The animals (n = 6) were prepared as described for Series 2. In addition, a catheter attached to a 22-gauge curved needle was inserted into the renal artery distal to the flow probe. After three 20-minute control periods, the priming dose of ANF peptide (2 μg/kg, i.v.) was given as described for Series 1 and 2. The sustained infusion of the peptide, however, was administered directly into the renal artery distal to the flow probe at a rate of 200 ng/kg/min for the two subsequent
20-minute experimental periods. This intrarenal approach was selected to produce a higher renal concentration of the peptide without increasing the systemic dose. This procedure minimizes potential systemic actions of the peptide that might occur with higher intravenous doses. After the infusion of ANF was stopped, two 20-minute recovery periods were obtained. In all other respects, the experimental protocol for Series 2 was followed.

**Analytical Methods**

Plasma renin activity in arterial and renal venous samples was measured by radioimmunoassay. The renin secretion rate, calculated by multiplying the difference between renal venous and systemic arterial plasma renin activity by renal plasma flow, is expressed as nanograms of angiotensin I per minute. Renal plasma flow was calculated from RBF and the hematocrit, which was determined by the microcapillary tube method. Plasma and urine electrolyte concentrations were determined by flame photometry. Plasma and urine creatinine were measured by standard colorimetric methods. The results are presented as means ± SEM. The data were analyzed by analysis of variance for repeated measurements and the least significant difference statistic. Student’s paired t test was also used where indicated. Differences at the 5% level were considered significant.

**Results**

In the three experimental series of this study, the baseline functions remained stable during the three control periods, and no statistical differences among the three control periods were noted for any of the functions studied. The one exception was urinary potassium excretion in Series 1.

**Series 1: Intravenous Infusion of Atrial Natriuretic Factor in Dogs with a Single Filtering Kidney**

The hemodynamic and renin secretion data are shown in Figure 1. In three control periods, MAP was 149 ± 5 mm Hg (see Figure 1, top panel). Infusion of ANF decreased MAP to 142 ± 7 and 140 ± 6 mm Hg during the first and second experimental periods, respectively (p < 0.05 for both values), and the significant decrement persisted throughout the two recovery periods. Control heart rates (data not shown) ranged from 153 ± 10 to 158 ± 9 beats/min and did not change significantly during the experiment. Baseline values for RBF ranged from 255 ± 36 to 275 ± 45 ml/min (Figure 1, middle panel). The bolus injection of ANF (2 μg/kg, i.v.) produced a transient increase in RBF from 275 ± 45 ml/min to a peak level of 353 ± 53 ml/min (p < 0.05 compared with the third control value, by paired t test). The average time for this peak response to occur was 43 ± 5 seconds after the bolus injection of ANF. Thereafter, RBF rapidly returned to control levels despite the sustained infusion of ANF peptide at 200 and 400 ng/kg/min for the next two 20-minute periods. Administration of ANF produced a marked inhibition of the renin secretory rate (see Figure 1, bottom panel). Baseline renin secretion rates ranged from 1083 ± 322 to 1313 ± 218 ng of angiotensin I per minute. Renin secretion decreased to 205 ± 120 and 286 ± 168 ng of angiotensin I per minute, respectively, during the two experimental periods (p < 0.05 for both values), with a mean fall of approximately 80%. After the ANF infusion was stopped, renin secretion returned to control levels, with values of 900 ± 446 and 1477 ± 594 nanograms of angiotensin I per minute during the first and second recovery periods, respectively.

The effects of ANF on creatinine clearance and renal excretory function are presented in Table 1. Infusion of ANF produced a significant increment in creatinine clearance—approximately 20% above control values. Similarly, the urine volume increased twofold (p < 0.05), and urinary sodium excretion increased threefold to fourfold (p < 0.05). The changes in creatinine clearance and urinary sodium excretion during ANF administration were associated with an increment of approximately 20% in the filtered load of sodium (p < 0.05) and a threefold to fourfold increment in the fractional excretion of sodium (p < 0.05). Baseline values of urinary potassium excretion were not stable, and a statistical difference was noted between the first and third control periods (p < 0.05). Infusion of ANF produced a 1.5-fold to two-fold increment in urinary potassium excretion (p < 0.05). The plasma sodium concentration did not change significantly during the experiment, but a slight decrement in the plasma potassium level occurred during the second experimental period (p < 0.05) and persisted during the two recovery periods. The hematocrit was 44 ± 3% and did not change significantly during the study.

**Series 2: Intravenous Infusion of Atrial Natriuretic Factor in Dogs with a Single Denervated Nonfiltering Kidney**

The hemodynamic and renin secretion data are presented in Figure 2. Control measurements of MAP ranged from 148 ± 7 to 149 ± 6 mm Hg (see Figure 2, top panel). Infusion of ANF decreased MAP to 142 ± 7 mm Hg during the second experimental period (p < 0.05), and MAP remained significantly decreased through the two recovery periods, at 143 ± 7 and 143 ± 8 mm Hg. Control heart rates (data not shown) ranged from 170 ± 8 to 173 ± 8 beats/min and did not change significantly during the experiment. During the control periods, RBF ranged from 83 ± 12 to 85 ± 14 ml/min (see Figure 2, middle panel). Bolus injection of ANF (2 μg/kg/min) increased the RBF from 84 ± 14 ml/min to a peak response of 121 ± 25 ml/min (p < 0.05 compared with the third control value, by paired t test). The average time for this peak response to occur was 43 ± 4 seconds after the bolus injection of the peptide. In contrast to the results in animals with a filtering kidney, in this series RBF did not return to control levels but remained significantly elevated dur-
FIGURE 1. Effects of intravenous infusions of synthetic atrial natriuretic factor (ANF) in anesthetized dogs with a single filtering kidney. A bolus of ANF (2 μg/kg, i.v.) was given at 60 minutes. Infusion of ANF was set at 200 ng/kg/min between 60 and 80 minutes and at 400 ng/kg/min between 80 and 100 minutes. Abbreviations: C1,2 = control periods; E1,2 = experimental periods; R1,2 = recovery periods; MAP = mean arterial pressure; RBF = renal blood flow; RSR = renin secretion rate; AI = angiotensin I. *p < 0.05; n = 6.

FIGURE 2. Effects of intravenous infusions of synthetic atrial natriuretic factor (ANF) in anesthetized dogs with a single denervated nonfiltering kidney. A bolus of ANF (2 μg/kg, i.v.) was given at 60 minutes. Infusion of ANF was set at 200 ng/kg/min between 60 and 80 minutes and at 400 ng/kg/min between 80 and 100 minutes. Abbreviations are the same as those in Figure 1. *p < 0.05; n = 6.
ANF was set at 200 ng/kg/min between 60 and 110 minutes. Intrarenal infusion of ANF also produced a striking inhibition of renin secretion in dogs with a single denervated nonfiltering kidney (see Figure 2, bottom panel). During the three control periods, renin secretion ranged from 263 ± 87 to 311 ± 98 ng of angiotensin I per minute and decreased to 72 ± 22 and 91 ± 37 ng of angiotensin I per minute, respectively, during the first and second experimental periods (p < 0.05 for both values), producing an average decrement of 71%. During the two recovery periods, renin secretion tended to return to control levels. Aortic constriction in four animals (data not shown) decreased renal perfusion pressure to an average of 76 ± 5 mm Hg, and this resulted in a striking increase in renin secretion, to 933 ± 174 ng of angiotensin I per minute (p < 0.05 by paired t test). Aortic constriction was not produced in two dogs because of technical difficulties.

Plasma sodium concentrations ranged from 144 ± 1 to 145 ± 1 mEq/L during the control periods and did not change significantly during the study. The plasma potassium level during the control periods ranged from 4.42 ± 0.09 to 4.48 ± 0.09 mEq/L and increased slightly but significantly, to a level of 4.59 ± 0.10 mEq/L during the second experimental period. In the recovery periods plasma potassium concentrations remained significantly higher than control values, at 4.60 ± 0.11 and 4.62 ± 0.12 mEq/L. The hematocrit was 44 ± 2% and did not change significantly during the study.

**Series 3: Intrarenal Infusion of Atrial Natriuretic Factor in Dogs with a Single Denervated Nonfiltering Kidney**

In this experimental series, ANF was infused intrarenally at 200 ng/kg/min, to study the effects that a higher renal concentration of the peptide would have on renal hemodynamics and renin secretion. The results of this experiment are presented in Figure 3. Control measurements of MAP ranged from 146 ± 4 to 147 ± 5 mm Hg (see Figure 3, top panel), and control heart rate values (not shown) ranged from 147 ± 12 to 150 ± 11 beats/min; neither variable changed significantly during or after administration of the ANF peptide. Baseline levels of RBF ranged from 79 ± 7 to 83 ± 6 ml/min (see Figure 3, middle panel). A bolus injection of ANF (2 μg/kg/min) increased the RBF from 83 ± 6 ml/min to a peak response of 124 ± 14 ml/min (p < 0.05 compared with the third control value, by paired t test), observed 47 ± 5 seconds after the peptide had been administered. Like the previous series, this series had significantly elevated RBF throughout the infusion of ANF, averaging 111 ± 7 and 113 ± 7 ml/min during the first and second experimental periods, respectively. Intrarenal infusion of ANF also produced a significant inhibition of renin secretion in these dogs (see Figure 3, bottom panel). Renin secretion ranged from 246 ± 48 to 291 ± 63 ng of angiotensin I per minute during the control periods and decreased to 126 ± 52 and 138 ± 52 ng of angiotensin I per minute during the first and second experimental periods, representing an average fall of 50%. In the first recovery period renin secretion remained suppressed at 132 ± 34 ng of angiotensin I per minute — a level that was still significantly decreased from the control value. Aortic constriction in the six dogs (data not shown) decreased renal perfusion pressure to 77 ± 6 mm Hg, and this produced a sixfold increment in renin secretion, from 167 ± 58 to 1080 ± 268 ng of angiotensin I per minute (p < 0.05 by paired t test). Baseline plasma sodium concentrations ranged from 143 ± 2 to 144 ± 2 mEq/L, and plasma potassium concentrations from 4.48 ± 0.22 to 4.54 ± 0.20 mEq/L. The levels of these electrolytes did not change significantly during the infusion or recovery periods. The hematocrit was 45 ± 1% and did not change significantly during the study.

**Figure 3.** Effects of intrarenal arterial infusions of synthetic atrial natriuretic factor (ANF) in dogs with a single denervated nonfiltering kidney. A bolus of ANF (2 μg/kg, i.v.) was given at 60 minutes. Intrarenal infusion of ANF was set at 200 ng/kg/min between 60 and 100 minutes. Abbreviations are the same as those in Figure 1. *p < 0.05: n = 6.
Discussion

Recent studies have reported a marked inhibitory action of several synthetic ANF peptides on the secretion of renin in anesthetized or conscious dogs, leading to the hypothesis that this inhibition of renin secretion was mediated in response to an ANF-induced increment in the sodium load delivered to the macula densa. Inhibition of renin release in the present study was also associated with increments in glomerular filtration and the tubular load of sodium chloride during infusion of the ANF peptide in dogs with a single filtering kidney. However, our results in the two experimental series with a single denervated nonfiltering kidney demonstrate for the first time, to our knowledge, the important biological action of ANF as an inhibitor of renin secretion in the absence of a functional macula densa mechanism. The findings in these two experimental series indicate that ANF-induced suppression of renin secretion can occur without an increment in the tubular load of sodium delivered to the macula densa. The mechanisms by which ANF suppressed renin secretion in dogs with a denervated nonfiltering kidney are unclear, but infusions of the peptide produced sustained renal arteriolar vasodilatation and increased RBF. Renal arteriolar dilation would be expected to provide an inhibitory signal from the renal vascular receptor to suppress renin release. Alternatively, ANF may have suppressed renin secretion by a direct action on the juxtaglomerular cells in both the series with a denervated nonfiltering kidney and the series with an intact filtering kidney. In this regard, recent in vitro studies by Obana et al. suggest that synthetic ANF peptides can inhibit renin release from kidney slices in a dose-dependent fashion. Thus, the present study indicates that ANF peptides influence renin secretion through potential interactions with the two intrarenal receptor mechanisms, the renal vascular receptor and the macula densa. The possibility that ANF also exerts a direct inhibitory action on the juxtaglomerular cells in vivo cannot be excluded.

Several synthetic ANF peptides have been reported to be selective renal vasodilators and to increase the RBF in both conscious and anesthetized dogs. In other studies with dogs, continuous infusion of synthetic ANF produced only transient increases in RBF, which returned to the preinfusion level after several minutes. Sustained ANF-induced increments in glomerular filtration were reported in those studies in which it was measured. The present results in dogs with a single intact kidney also indicate a sustained ANF-induced elevation in glomerular filtration, together with a transient increment in the RBF during continuous infusion of the peptide. In contrast, ANF-induced increments in RBF were sustained throughout the entire ANF infusion period in the dogs with a single denervated nonfiltering kidney, and the RBF in these animals returned to baseline values only after infusion of the peptides had been stopped.

The reasons for the difference in the steady-state RBF response to ANF infusion between the dogs with an intact filtering kidney and those with a denervated nonfiltering kidney are unclear. One possible explanation, however, might be related to the absence of a functional tubuloglomerular feedback mechanism in the dogs with a nonfiltering kidney. In normal animals with intact kidneys, increased delivery of solute and fluid to the distal nephron segments activates a tubuloglomerular feedback mechanism, which increases afferent and efferent arteriolar resistance and thereby reduces renal plasma flow and glomerular filtration. In the present study, increased tubular fluid and solute delivery could not occur during ANF infusion in the dogs with a nonfiltering kidney. Consequently, the renal vasodilating action of ANF was not opposed by the physiological vasoconstriction resulting from the activation of a tubuloglomerular feedback mechanism to initiate adjustments in renal arteriolar tone. Thus, a sustained increase in renal blood flow during infusion of synthetic ANF occurred in this experimental series. Presumably, the tubuloglomerular feedback mechanism was partially activated to adjust renal arteriolar tone in response to ANF-induced increments in solute and fluid delivery in the dogs with an intact filtering kidney. Alternatively, the sustained vasodilating action of ANF in the dogs with a nonfiltering kidney may be related to the baseline renal vascular resistance in these animals. It has been suggested that preconstricted renal arterioles are more responsive to ANF-induced vasodilatation. In the present study the baseline renal vascular resistance was approximately threefold higher in the dogs with nonfiltering kidneys than in those with intact filtering kidneys.

Creatinine clearance increased significantly in the dogs with intact kidneys during the infusion of ANF in the present study. Since this sustained increase in creatinine clearance occurred despite a slight decrease in arterial pressure and no sustained increment in RBF, it may be related to an increase in glomerular capillary permeability. Alternatively, ANF may increase glomerular filtration by selectively altering segmental renal arteriolar resistance to increase the glomerular capillary pressure. In preliminary studies involving direct measurement of glomerular capillary hydrostatic pressure in Munich-Wistar rats, ANF-induced increases in hydrostatic pressure were associated with renal afferent arteriolar dilation and efferent arteriolar constriction. In addition, the increase in glomerular filtration may be related to a redistribution of blood flow within the kidney during infusion of ANF peptides. Our study does not provide sufficient evidence to permit a distinction among these alternatives.

In the present study the dogs with an intact kidney had brisk diuresis, natriuresis, and kaliuresis during infusion of the ANF peptide. This response was associated with an increase in the creatinine clearance and the filtered loads of solute and fluid presented to the tubules. This relationship between the renal hemodynamic responses to ANF peptides and the natriuretic-diuretic responses has been emphasized by several groups. The present results indicate, however, that marked natriuresis and diuresis persisted during
Thus, the natriuretic-diuretic response to the ANF peptide cannot be fully explained on the basis of increased glomerular filtration. This observation may suggest that ANF inhibits sodium reabsorption through a tubular action. Hammond et al.\(^1\) have reported that a synthetic ANF peptide inhibits proximal tubular transport of sodium which is linked to the tubular reabsorption of phosphate and bicarbonate. Reported increments in the clearance and excretion of lithium during infusion of ANF peptide also point to a proximal tubular effect.\(^11\) In addition, it has been suggested that ANF peptides inhibit tubular sodium reabsorption in more distal segments of the nephron.\(^10,13\) The quantitative contributions of these different mechanisms to ANF-induced alterations in solute and fluid excretion are unknown.

Arterial pressure decreased slightly but significantly during intravenous infusion of the ANF peptide in Series 1 and Series 2, and there was no reflex tachycardia associated with the response in either series. Arterial pressure did not change during intrarenal arterial infusion of the peptide in Series 3, although striking renal vasodilation occurred in these animals. Previous studies have demonstrated that atrial extracts and ANF peptides produce relaxation of isolated vascular smooth muscle preparations.\(^20,30-32\) suggesting that the depressor response observed in our study may be due in part to vasodilation and a decrease in peripheral resistance. It has been reported, however, that intravenous infusions of ANF peptide in conscious rats produced dose-dependent increases in MAP and cardiac output.\(^33\) Thus, the ANF-induced depressor response in the present study may be due to one or both of these cardiovascular effects of the peptide.

In summary, infusion of synthetic ANF peptide produced significant inhibition of renin secretion in dogs with either an intact kidney or a single denervated nonfiltering kidney. Inhibition of renin secretion was associated with increments in creatinine clearance and the filtered load of sodium presented to the renal tubules in the dogs with intact kidneys. Inhibition of renin secretion was associated with sustained renal vasodilation in the dogs with nonfiltering kidneys. We conclude that ANF-induced inhibition of renin secretion is mediated through its interactions with the two intrarenal receptor mechanisms, the renal vasoreceptor and the macula densa. A direct inhibitory action of ANF peptide on the juxtaglomerular cells is also possible.

### References

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