Role of Pressure Natriuresis in Long-term Control of Renal Electrolyte Excretion

H. Leland Mizelle, Jean-Pierre Montani, Robert L. Hester, Ralph H. Didlake, John E. Hall

If pressure natriuresis is to play an important role in arterial pressure control, renal perfusion pressure must have a long-term effect on urinary sodium excretion. The aim of this study was to quantitate the importance of renal perfusion pressure per se in controlling renal hemodynamics and electrolyte excretion chronically. Female mongrel dogs (n=6) were instrumented with bilateral renal artery catheters for measurement of renal perfusion pressure and occluders on both renal arteries for servo-control of renal perfusion pressure at different levels; the urinary bladder was split for determination of renal clearances and electrolyte excretion from each kidney separately. Because both kidneys were exposed to the same neurohumoral influences, any changes in renal function could be attributed to differences in renal perfusion pressure between the two kidneys. After 5 days of control, renal perfusion pressure to one kidney was reduced from 86.7±0.2 to 74.2±0.6 mm Hg for 12 days, and pressure in the contralateral kidney increased to 91.5±0.4 mm Hg. Sodium excretion decreased from 41±2 to 25±1 mmol/d in the servo-controlled kidney and increased from 41±1 to 55±1 mmol/d in the contralateral kidney during 12 days of servo-control. Urine volume, chloride excretion, and potassium excretion exhibited similar patterns during servo-control. In addition, autoregulation of effective renal plasma flow and glomerular filtration rate was relatively well maintained; however, in the low-pressure kidney, glomerular filtration rate was slightly but significantly lower (~8%) than in the contralateral kidney. In summary, long-term changes in renal perfusion pressure caused sustained alterations in renal electrolyte excretion. These results suggest that renal perfusion pressure is an important long-term controller of sodium and water excretion. (Hypertension 1993;22:102-110)

KEY WORDS • natriuresis • sodium • renal circulation • glomerular filtration rate • blood pressure • hypertension, renovascular

Arterial pressure is maintained relatively constant over the long-term by complex interactions between the various neurohumoral control systems and the ability of the kidneys to excrete salt and water. Guyton and colleagues1 (see References 2 through 5 for review) have emphasized renal–body fluid feedback as the dominant control system for long-term blood pressure control. A key component of this feedback is the effect of arterial pressure on renal excretion of sodium, often referred to as pressure natriuresis. In most instances, this mechanism is believed to stabilize blood pressure in response to various perturbations that would tend to cause hypertension or hypotension.

The validity of this concept depends on the assumption that arterial pressure has a long-term influence on renal excretion of sodium and water, a premise that has been difficult to test experimentally. Numerous investigators have demonstrated that acute changes in arterial pressure markedly alter sodium and water excretion,6-9 but the long-term effects of pressure per se on renal excretion are largely unknown. Long-term pressure-natriuresis curves are usually determined indirectly by measuring the steady-state arterial pressure in response to long-term changes in salt intake from very low to very high levels.1,10-12 These salt-loading pressure-natriuresis curves are a function of not only pressure but also changes in various other factors such as alterations in circulating angiotensin II. In fact, one of the reasons it is difficult to determine the long-term effects of pressure per se is that any attempt to induce a primary change in arterial pressure chronically almost invariably leads to compensatory changes in various neurohumoral systems that tend to alter renal excretion and restore arterial pressure back to normal.

In contrast, some investigators contend that the renal–body fluid feedback concept is invalid because the kidneys reset their excretion of sodium and water so that balance between intake and output can be maintained independently of pressure.13-15 If the kidneys adapt to changes in arterial pressure, pressure natriuresis would not be a major long-term controller of blood pressure. This adaptation, however, has not been demonstrated experimentally. In fact, no previous studies, to our knowledge, have directly examined the long-term effects of pressure on renal excretion.

Therefore, the purpose of this study was to quantitate the effects of renal perfusion pressure per se on long-term excretion of water and electrolytes. This was done by chronically altering renal perfusion pressure of the two kidneys (in the same animal) to different levels while using a split bladder technique to determine renal
hemodynamics and excretory function of each kidney separately.

Methods

Surgical Procedures

The experimental protocols for this study were approved by the Institutional Animal Care and Use Committee of the University of Mississippi Medical Center and were carried out according to the Guide for the Care and Use of Laboratory Animals from the National Institutes of Health and according to the guidelines of the Animal Welfare Act.

Experiments were conducted in six female mongrel dogs with body weights ranging from 18.2 to 21.8 kg (average, 19.5±0.6 kg). All surgical procedures were performed during sodium pentobarbital anesthesia (30 mg/kg) with aseptic technique, and butorphanol (0.3 mg/kg) was used for postoperative analgesia. Tygon catheters (Norton Plastics and Synthetics Division, Akron, Ohio) were implanted in the femoral arteries and veins to allow easy access to blood samples and to provide a route for intravenous infusions. On the same day, the urinary bladder was split by a modification of our previously described technique. Briefly, the bladder was accessed via a midline abdominal incision, and the urethra was tied. The bladder was divided approximately three fourths the length from the fundus toward the neck of each hemibladder were closed using 3-0 Vicryl suture (Ethicon Inc, Somerville, NJ). The bladder catheters were implanted through a stab wound near the fundus of each hemibladder and secured with a purse string suture (4-0 Ethibond). The catheters were exteriorized across the abdominal wall and connected to sterile plastic bags as previously described. Approximately 1 week later, left and right retroperitoneal flank incisions were performed, and a silicone elastomer occluder was placed around each renal artery near its origin from the aorta. In addition, small-bore (nonobstructive) catheters were implanted into both renal arteries distal to the occluder to allow measurement of the renal perfusion pressure of each kidney. The catheters and occluder tubing were tunneled subcutaneously and exteriorized in the scapular region. Before the dogs were placed in metabolic cages, patency of the renal artery catheters was maintained by flushing daily with sterile isotonic saline and filling the catheters with heparin (1000 U/mL). All dogs were given daily antibiotics throughout the experiment (amoxicillin, di-cloxacillin, and a trimethoprim and sulfamethoxazole combination), and rectal temperatures were monitored to ensure the dogs were afebrile during the study.

Twenty-four-Hour Monitoring Procedure

The dogs were housed in metabolic cages in an air-conditioned room with a 12-hour light cycle and fitted with harnesses containing flow-through pressure transducers (Cobe, Lakewood, Colo) mounted at heart level. Each renal arterial catheter was connected to a syringe pump (model 944, Harvard Instruments, South Natick, Mass) that was used to infuse isotonic heparinized saline (20 U/mL heparin) at a rate of approximately 41 mL/d into each renal artery during the entire experiment to maintain the renal artery catheters patent. The solution was pumped through a high-resistance line (Tygon, 0.02-in id) into the flow-through pressure transducer and then into the dog's catheter. Renal arterial pressure was continuously recorded on a polygraph (model 7D, Grass Instrument Co, Quincy, Mass). The renal arterial pressure signals from the Grass recorder were sent to an analog-to-digital converter and analyzed with a microcomputer (AT&T PC 6300) as previously described. In addition, each minute, the values for renal arterial pressure, heart rate, and pulse pressure were sent through a serial line to a second microcomputer in the laboratory that was connected to a modem. Customized software on this computer kept a running tabulation of the last 720 minutes of data and compared each incoming data point to preset error limits. If the latest values fell outside the acceptable boundary, the modem was activated to call a pager carried by the investigator. This allowed any problems to be corrected quickly, even during late-night hours. Because renal clearances were not determined every day and because all routine care of the dogs, including changing urine bags, feeding, and cleaning cages, was conducted between the hours of 8 AM and noon, the average daily pressure was calculated from the values recorded between the hours of noon and 8 AM. These reported values give a more consistent determination of mean arterial pressure that can be compared from day to day. However, it should be emphasized that during the experimental period the renal perfusion pressure was still servo-controlled 24 hours per day.

After the animals were placed in metabolic cages, one of the venous lines was connected to a roller pump (model 375A, Sage Instruments, Cambridge, Mass) that was used to infuse isotonic saline at a rate of approximately 407 mL/d during the entire experiment. All infusions were pumped through a filter (0.22-μm Cathived, Millipore Corp, Bedford, Mass) to prevent bacteria and contaminants from passing into the circulation. The dogs were allowed free access to tap water and fed a low-sodium dog food (H/D, Hill's Pet Products, Topeka, Kan), containing approximately 5 to 6 mmol sodium per day. The average total sodium intake was fixed at 81 mmol/d throughout the experiment.

Experimental Protocol

After the dogs had been in the harnesses for 7 to 10 days, control measurements were begun. After at least 5 consecutive days of control, renal perfusion pressure to one kidney was servo-controlled at a level that averaged 13 mm Hg less than the control pressure, and renal perfusion pressure in the contralateral kidney was allowed to vary with systemic arterial blood pressure. The renal perfusion pressure was continuously servo-controlled 24 hours per day for 12 days as previously described. At the end of the 12th day, the servo-controller was stopped, and measurements were continued for an additional 7 days. Servo-control of the right or left kidney was randomized.
Daily excretions of water, sodium, potassium, and chloride were determined throughout the experiment. Renal clearances, plasma renin activity (PRA), plasma aldosterone concentration, and plasma atrial natriuretic peptide (ANP) levels were measured on 2 different days of the control period; on days 2, 5, 7, 9, and 12 of servo-control; and on days 2 and 4 of recovery.

Control renal plasma flow (ERPF) and effective renal plasma flow (ERPF) were estimated from the 24-hour clearances of \([125I]\)iodohippurate (Glofil, Isotex Diagnostics) and \([131I]\)iodohippurate (Bristol-Myers Squibb, Princeton, NJ), respectively. On the day of the determination of renal clearances, a bolus of 20 \(\mu\)Ci of \([125I]\)iodohippurate and 50 \(\mu\)Ci of \([131I]\)iodohippurate was injected at least 1 hour before the normal time for changing the urine bags. Immediately after injection of the bolus, the intravenous infusion bags were changed and replaced with bags containing isotope providing a continuous infusion of \([125I]\) and \([131I]\) at rates of 0.05 and 0.1 \(\mu\)Ci/min, respectively. After 1 hour of equilibration, the urine bags were changed and the 24-hour clearance was begun. Plasma samples were taken at 2, 4, and 22 hours after the clearance period was begun, and the urine was collected after 24 hours. Renal clearances were calculated as \(U_c \cdot V/P_c\), where \(U_c\) is the counts per minute per milliliter in the urine, \(V\) is the urine flow rate in milliliters per minute, and \(P_c\) is the average counts per minute per milliliter of the plasma samples.

Analytical Methods

Urine sodium and potassium concentrations were determined by ion-selective electrodes (Nova 1+1 Na-K Analyzer, Nova Biomedical, Waltham, Mass.), and chloride was measured by titration (Haake-Buchler chloridometer, Saddle Brook, NJ). \(125I\) and \(131I\) were counted on a gamma counter (model 1185, Searle, Des Plaines, Ill.). PRA, plasma aldosterone concentration, and plasma ANP were measured by radioimmunoassay.

At the end of the experiment, the dogs were euthanized by an overdose of sodium pentobarbital, and both hemibladders were examined for lesions in the mucosa and for muscle hypertrophy. The kidneys were examined to ensure that there was no damage due to autoregulation for up to 12 days of reduced renal perfusion pressure. Sodium and potassium excretion were also sensitive to the changes in renal perfusion pressure. Sodium excretion fell significantly from an average of 41 ±2 to 25 ±1 mmol/d in the low-pressure kidneys and increased significantly from 41 ±1 to 55 ±1 mmol/d in the contralateral kidneys. When the servo-controller was stopped, sodium excretion in the two kidneys returned to control levels, averaging 43 ±2 and 42 ±2 mmol/d. The sodium retention in the low-pressure kidneys was exactly counterbalanced by the natriuresis in the contralateral kidneys such that overall sodium balance was not significantly different among the control, experimental, or recovery periods. Sodium balance averaged -1 ±3 mmol/d during control, 0 ±2 mmol/d during the 12 days of reduced renal perfusion pressure, and -4 ±3 mmol/d during recovery.

As shown in Fig 2, chloride and potassium excretions were also sensitive to the changes in renal perfusion pressure, although the effects on potassium excretion were not as dramatic. Chloride excretion changed significantly from an average of 64 ±2 and 65 ±1 to 43 ±1 and 86 ±2 mmol/d in the low-pressure and contralateral kidneys, respectively. In the recovery period, chloride excretion returned to control values, averaging 66 ±1 and 67 ±2 mmol/d. Potassium excretion in the low-pressure kidneys fell significantly from 34 ±1 to 27 ±0 mmol/d, and in the contralateral kidneys it significantly increased from 34 ±1 to 39 ±0 mmol/d, with both kidneys returning to control in the recovery period.

Fig 3 illustrates the renal hemodynamic responses to long-term changes in renal perfusion pressure. There were no significant differences in ERPF between the low-pressure and contralateral kidneys during any experimental period, indicating effective renal blood flow autoregulation for up to 12 days of reduced renal perfusion pressure. During control, the 24-hour ERPF averaged 61 ±3 mL/min in the servo-controlled kidneys and 62 ±3 mL/min in the contralateral kidneys. In the low-pressure kidneys ERPF was 92 ±2% of control, and in the contralateral kidneys ERPF averaged 93 ±2% of control during the experimental period. During recovery, ERPF was 100 ±1% and 104 ±3% of control in the low-pressure and contralateral kidneys, respectively. The apparent slight fall in ERPF in both kidneys during the servo-control period did not reach statistical significance. The 24-hour GFR was 22 ±1 mL/min in the low-pressure kidneys and 22 ±1 mL/min in the contralateral kidneys during the control period. GFR was slightly, but significantly, lower in the low-pressure kidneys during servo-control, averaging 85 ±1% of control, whereas the contralateral control kidneys averaged 93 ±2% of control (Fig 3). This value was not significantly different from control. GFR averaged 92 ±1% and 90 ±3% of control during the recovery period in the control and servo-controlled kidneys, respectively.
Plasma electrolyte concentrations remained stable throughout the experiment; during the control period, plasma sodium averaged 146.5±0.6 mmol/L, plasma potassium was 4.97±0.17 mmol/L, and plasma chloride was 115.0±0.4 mmol/L.

Fractional excretions of sodium, chloride, and potassium paralleled the changes in absolute excretion (Fig 4). Fractional excretion of sodium was 0.94±0.05% and 0.95±0.02% during the control period and fell significantly to 0.64±0.06% in the low-pressure kidneys and increased significantly to 1.37±0.08% in the contralateral kidneys. During the recovery period, fractional excretion of sodium averaged 1.02±0.00% and 1.02±0.01%. Fractional excretion of chloride followed the same pattern, falling significantly from 1.81±0.07% to 1.44±0.12% in the low-pressure kidneys and significantly increasing from 1.85±0.02% to 2.66±0.08% in the contralateral control kidneys (Fig 4). Both kidneys returned to control levels when the servo-controller was stopped. The effects on fractional excretion of potassium were not as dramatic. Fractional excretion of potassium in the low-pressure kidneys did not change significantly, averaging 21.5±0.5% during control, 20.3±0.3% during servo-control, and 22.4±0.3% during recovery. However, in the contralateral kidneys, fractional excretion of potassium increased significantly from 21.5±0.9% to 26.9±0.5% during servo-control and returned to 22.9±0.1% during recovery.

PRA significantly increased from an average of 0.21±0.02 to 0.49±0.04 ng angiotensin I/mL per hour during servo-control. PRA averaged 0.38±0.08 ng angiotensin I/mL per hour during the recovery period. Plasma aldosterone concentration averaged 3.2±0.7, 3.1±0.2, and 2.3±0.2 ng/dL during control, servo-control, and recovery, respectively. Plasma ANP (determined in four of the six dogs) averaged 54.3±5.6 pg/mL during control and 73.5±3.8 pg/mL during the 12 days of servo-control. During recovery, plasma ANP was 52.7±2.4 pg/mL.

Discussion

The most important finding of this study is that long-term changes in renal perfusion pressure per se
caused long-term alterations in excretion of water, sodium, chloride, and, to a lesser extent, potassium for as long as the renal perfusion pressure was altered. Renal pressure was reduced by approximately 13 mm Hg to one kidney, while pressure in the contralateral kidney was allowed to vary with the systemic arterial pressure and increased approximately 4 mm Hg. In addition, autoregulation of renal hemodynamics was effective in response to the changes in perfusion pressure, and overall sodium balance was maintained. Although it is well known from short-term studies that acute changes in renal perfusion pressure can dramatically alter renal excretion of water and electrolytes, to our knowledge this is the first study to examine directly the long-term effects of renal perfusion pressure per se on renal excretion.

This study provides strong evidence in support of the renal–body fluid feedback concept of long-term blood pressure control (see References 2 through 5 for review). The crucial component of this feedback that allows the kidneys to control arterial pressure is the effect of renal perfusion pressure on excretion of sodium, i.e., pressure natriuresis. Some investigators, however, have suggested that pressure-induced natriuresis is only a transient phenomenon. This hypothesis suggests that, after long-term changes in blood pressure, the kidneys reset their excretion to the new pressure level, allowing electrolyte balance to be maintained independently of pressure. If this were true, pressure natriuresis would be unimportant in determining the long-term arterial pressure level. However, we have clearly demonstrated in this study that pressure does indeed have a long-term influence on renal excretion of water and electrolytes. Sodium, water, chloride, and potassium excretions were significantly reduced in the kidney exposed to low pressure and significantly increased in the contralateral kidney for as long as the pressure differential was present (12 days). These data suggest that renal excretion is strongly influenced by the level of perfusion pressure and contradict the notion that the kidneys intrinsically adapt to changes in perfusion pressure.

Another important implication of the renal–body fluid feedback concept of arterial pressure control is that hypertension will not occur unless there is a shift in the pressure-natriuresis relation such that higher perfusion pressures are required to excrete a given amount of sodium. Therefore, a necessary prerequisite to hyper-
tension would be a reduction in the ability of the kidneys to excrete sodium and water at normal pressure. In support of this idea, previous studies have found that pressure also has important long-term effects on sodium excretion in various models of experimental hypertension.\textsuperscript{20,21} (see Reference 5 for review). For example, an increase in renal perfusion pressure was essential in offsetting the sodium-retaining actions of long-term infusions of aldosterone or angiotensin II.\textsuperscript{20,21} When renal perfusion pressure was prevented from increasing as hypertension developed, sodium retention continued, and in some experiments the extracellular fluid volume expansion that occurred resulted in severe circulatory disturbances such as pulmonary edema, ascites, or both. However, these studies did not quantitate the importance of renal perfusion pressure per se on renal function. It is likely that there were major differences in neurohumoral compensations and other important factors, such as changes in body fluid volumes between the control animals and animals in which renal perfusion pressure was not allowed to increase during hypertension. In fact, these experiments underscore the difficulties involved in studying the long-term effects of pressure per se on renal excretion. In the present study, we were able to control for systemic changes (eg, circulating hormones, sympathetic activity) because renal perfusion pressure was reduced to one kidney while pressure in the contralateral kidney was allowed to vary with systemic arterial pressure. Therefore, both kidneys were exposed to the same neurohumoral influences; thus, this is a powerful model because the differential excretion can be attributed to the changes in perfusion pressure or intrarenal mechanisms activated by changes in perfusion pressure.

This model is, in some ways, similar to the two-kidney, one clip (2K1C) model that is often used in hypertension studies. In the 2K1C model, there is a pressure differential between the clipped and unclepped kidneys, and previous studies that have examined separate renal function acutely have found results similar to ours.\textsuperscript{22,23} However, in the 2K1C model there is a fixed stenosis on one renal artery; therefore, when the systemic arterial pressure increases, the pressure beyond the clip increases. Consequently, renal perfusion pressure to the clipped kidney changes with time, not only chronically as the hypertension develops but also with
the fluctuations in blood pressure that occur during normal daily activity. This prevents determination of the quantitative long-term relation between renal perfusion pressure and sodium excretion in the 2K1C model. In contrast, the pressure distal to the occluder is prevented from increasing in our model because the servo-control unit adjusts the inflation of the occluder around the renal artery as the pressure changes. As a consequence, the renal perfusion pressure can be fixed and maintained at the desired level in spite of possible changes in systemic arterial pressure. The combination of the ability to chronically servo-control renal perfusion pressure of two kidneys (in the same animal) at different pressures and to determine renal hemodynamics and excretory function of each kidney separately has provided us with a unique way to study the long-term pressure-natriuresis relation.

The possible mechanisms responsible for short-term pressure natriuresis have been the subject of intense investigation during the past several years (see References 24 through 27 for review). One current hypothesis emphasizes alterations in intrarenal physical factors as the link between changes in renal perfusion pressure and tubular reabsorption of sodium. During increases in renal perfusion pressure, total renal blood flow is auto-regulated; however, it has been suggested that flow in the vasa recta increases in response to elevated perfusion pressure.28-30 This is accompanied by increases in vasa recta pressures and reduced fluid uptake by the vasa recta, resulting in increased medullary interstitial hydrostatic pressure that is transmitted throughout the kidney.28-30 Correlations between renal interstitial hydrostatic pressure and pressure natriuresis have been reported in hypertensive rat models31-33 and in dogs.34 Moreover, preventing changes in renal interstitial hydrostatic pressure by renal decapsulation tends to blunt the acute pressure-natriuresis response.28,31,34-37 Additionally, direct increases in renal interstitial hydrostatic pressure, within the range seen during changes in perfusion pressure, cause significant increases in sodium excretion.38,39 The nephron sites responsive to changes in interstitial pressure are most likely the proximal tubules and the descending limb of the loop of Henle, with deep nephrons being more sensitive than superficial nephrons.29-41 However, a few investigators have suggested that there may also be some effect of renal perfusion pressure in more distal nephron segments.42-43 Therefore, it seems likely that at least part of
the short-term pressure-natriuresis response may be due to the effects of alterations in renal medullary hemodynamics and interstitial hydrostatic pressure on tubular handling of electrolytes. The intrarenal mechanisms responsible for the long-term pressure natriuresis observed in the present study are unclear. However, it is possible that the alterations in renal medullary hemodynamics and interstitial hydrostatic pressures observed acutely are maintained as long as the pressure differential is present. It is interesting to note that in our experiments there were no differences in total ERPF between the low-pressure and contralateral kidneys during servo-control, indicating efficient renal blood flow autoregulation for as long as 12 days. GFR was also autoregulated in the contralateral kidneys during the 12 days of reduced renal perfusion pressure. However, GFR tended to fall slightly in the low-pressure kidneys during servo-control. The reduction in GFR may have contributed to the antinatriuresis in the low-pressure kidneys; however, fractional excretion of sodium still decreased markedly, indicating that there was an important increase in fractional reabsorption of sodium. Sodium excretion in the contralateral kidneys increased in spite of the tendency for GFR to be slightly lower than the control levels (not statistically significant). Therefore, the pressure natriuresis in the contralateral kidneys was probably not due to changes in filtered sodium load but more likely resulted from decreased tubular reabsorption.

Another important observation was the persistent natriuresis in the contralateral kidney in spite of a significant increase in systemic angiotensin II concentrations. PRA increased significantly during 12 days of reduced renal perfusion pressure, and the resulting increase in angiotensin II may have contributed to the increase in systemic arterial pressure. Interestingly, the contralateral kidneys were still able to increase their excretion of water and electrolytes in the face of the sodium-retaining influences of increased circulating angiotensin II concentrations. However, it is possible that the intrarenal levels of angiotensin II may have been different between the two kidneys. The servo-controlled kidney was exposed to a decrease in pressure and a small but significant decrease in GFR, both of which may have stimulated renin release. In contrast, the contralateral kidney was exposed to a slightly elevated pressure and normal renal blood flow and GFR. Therefore, it is possible that the intrarenal levels of angiotensin II were elevated in the low-pressure kidneys and suppressed in the contralateral kidneys. It is also conceivable that the differential pressures between the kidneys may have triggered differences in concentrations of other intrarenal hormones or possibly altered the sensitivities of the kidneys to various hormones. However, further studies are needed to test these possibilities. Additionally, these studies were carried out in dogs with intact renal nerves. This raises the possibility that the changes in pressure may have activated a renorenal reflex to alter contralateral renal function. However, this is very unlikely because, in dogs, studies have shown that raising renal venous pressure up to 28 mm Hg failed to activate a renorenal reflex. In fact, increasing ureteral pressure to approximately 63 mm Hg elicited only very small changes in contralateral renal blood flow (approximately −3%) and sodium excretion (approximately −10%). In addition, attempts to elicit a renorenal reflex via chemoreceptor stimulation by retrograde ureteropelvic perfusion with 0.9 M NaCl failed to produce any changes in contralateral renal function. Therefore, based on the available evidence, it seems likely that the neural influences are the same to each kidney under the conditions of our experiment.

In summary, long-term reductions in renal perfusion pressure to one kidney markedly decreased water and electrolyte excretion in the low-pressure kidney as long as the pressure was reduced. Systemic blood pressure increased slightly, and the contralateral kidney increased its excretion so that overall balance was maintained. We conclude that renal perfusion pressure has a potent long-term effect on renal excretion of water and electrolytes independent of changes in systemic levels of circulating hormones. This study provides strong evidence to support the concept that the pressure-natriuresis mechanism is an important means whereby the kidneys ultimately control the long-term level of arterial blood pressure.

Acknowledgments

This work was supported by grants HL-23502, HL-39399, and HL-11678 from the National Institutes of Health, Bethesda, Md.

We thank Calvin Torrey and Ken McDiwt for expert technical assistance. We also thank Lucille Sausen and United States Surgical Corp. for use of the GIA 90 Premium and the generous supply of reloads. We appreciate the work of Dr Manis J. Smith, Jr, who supervised the assays for PRA, plasma aldosterone concentration, and plasma ANP.

References

Role of pressure natriuresis in long-term control of renal electrolyte excretion.
H L Mizelle, J P Montani, R L Hester, R H Didlake and J E Hall

Hypertension. 1993;22:102-110
doi: 10.1161/01.HYP.22.1.102

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1993 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/22/1/102

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/