Relation Between Vasa Recta Blood Flow and Renal Interstitial Hydrostatic Pressure During Pressure Natriuresis

Emanuel Farrugia, John C. Lockhart, and Timothy S. Larson

Pressure natriuresis may be mediated through increases in inner medullary vasa recta blood flow (Q_{VR}). By means of acute renal decapsulation to prevent increases in renal interstitial hydrostatic pressure (RIHP), the effect of increases in Q_{VR} in the presence and absence of changes in RIHP in the natriuretic and diuretic responses to increases in renal perfusion pressure (RPP) was evaluated. Blood flow in descending (Q_{DVR}) and ascending (Q_{AVR}) vasa recta was determined in the exposed papilla by fluorescence videomicroscopy in anesthetized euvolemic Munich Wistar rats. In rats with intact renal capsules (n=12), increases in RPP from 101±0.5 to 132±2.9 mm Hg caused significant increases in Q_{DVR} (from 4.7±0.9 to 5.5±0.9 nl/min, p<0.001) and Q_{VR} (from 2.8±0.2 to 3.5±0.2 nl/min, p<0.001) in association with increases in RIHP (from 4.6±1.3 to 7.6±1.3 mm Hg, p<0.001), urine flow (from 16.2±2.6 to 20.2±3.2 μl/minemensal g kidney wt^{-1}, p<0.01), and urinary sodium excretion (from 2.10±0.38 to 3.36±0.62 μeq min^{-1}·g kidney wt^{-1}, p<0.001). Acute bilateral renal decapsulation (n=12) prevented the rise in RIHP (from 4.0±0.6 to 3.6±0.6 mm Hg), urine flow (from 13.0±2.1 to 14.2±1.5 μl/minemensal g kidney wt^{-1}), and urinary sodium excretion (from 1.76±0.28 to 2.12±0.31 μeq min^{-1}·g kidney wt^{-1}) as RPP increased from 100±0.3 to 134±2.2 mm Hg but not the increase in either Q_{DVR} (from 4.4±0.5 to 5.1±0.5 nl/min, p<0.01) or Q_{VR} (from 2.6±0.3 to 3.3±0.3 nl/min, p<0.001). No changes in Q_{DVR}, Q_{VR}, RIHP, urine flow, and fractional excretion of sodium were observed in a third group of time control decapsulated rats (n=7) in which RPP was held constant at 100 mm Hg. Glomerular filtration rate and total renal blood flow were stable in all three groups. These findings demonstrate that Q_{VR} increases in response to elevations in RPP but only results in natriuresis when associated with a concomitant rise in RIHP.

(Circulation Research 1992;71:1153–1158)

**KEY WORDS** vasa recta • pressure natriuresis • fluorescence videomicroscopy • renal interstitial hydrostatic pressure

Acute increases in renal perfusion pressure (RPP) have been shown to cause natriuresis and diuresis in the absence of detectable changes in total renal blood flow, glomerular filtration rate, or cortical peritubular capillary hydrostatic pressure.1–3 Although this effect of RPP is well recognized and plays an integral role in the regulation of extracutaneous fluid volume and arterial pressure,4 its mechanism(s) remains controversial. Changes in medullary blood flow in the setting of auto-regulated cortical and total renal blood flows have been proposed to play an important role in the pressure natriuresis phenomenon.5–7 Selkurt et al7 suggested that increases in medullary blood flow caused by elevations in RPP “wash out” the corticomedullary solute gradient and, in so doing, inhibit sodium reabsorption from the loop of Henle. Alternatively, it has been proposed that increases in medullary blood flow caused by elevations in RPP are transmitted into the renal medullary interstitium.5,6 The consequent rise in medullary renal interstitial hydrostatic pressure (RIHP) is distributed throughout the whole kidney and inhibits net sodium reabsorption in both superficial and deep nephrons, resulting in a natriuresis.6 Thus, a direct causal link may exist between increases in RPP, medullary blood flow, RIHP, and urinary sodium excretion (U_{NaV}). In support of this hypothesis, Roman et al10 have shown that elevations in renal papillary blood flow produced by increased RPP were associated with parallel increases in vasa recta capillary pressure, RIHP, and U_{NaV}.

There are, however, several considerations regarding the role of the medullary microcirculation during pressure natriuresis. Contrary to findings by Roman et al,10 others have demonstrated efficient autoregulation of inner medullary vasa recta blood flow (Q_{VR}).11,12 Also, it is possible that any observed increases in Q_{VR} occur as a consequence rather than as a cause of natriuresis and diuresis.13 Finally, the relation between increases in Q_{VR} and RIHP during pressure natriuresis has not been elucidated. Accordingly, the objective of this study was to test the hypothesis that elevations in RPP increase Q_{VR}, which results in natriuresis through increases in RIHP. By means of acute renal decapsulation that

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Received August 6, 1991; accepted July 9, 1992.
Prevented increases in RIHP, the effect of increases in QVR in the presence and absence of changes in RIHP in the natriuretic and diuretic responses of the Munich Wistar rat during elevations in RPP was evaluated.

Materials and Methods

Preparation of Animals

Young male Munich Wistar rats were purchased from Harlan Sprague Dawley, Inc., Indianapolis, Ind., and fed normal Purina rat chow containing 0.1 meq sodium/g. When these rats weighed approximately 80–90 g, a polyethylene matrix (to be used later for the continuous measurement of RIHP) was implanted in the dorsal aspect of the lower pole of the left kidney. Matrices were implanted in the kidney in proximity to the corticomedullary junction. The method of implantation and a detailed description of the polyethylene matrix are published elsewhere. One to 2 weeks later, the animals were prepared for videomicroscopy. The rats were fasted overnight but had free access to water before the experiment. They were anesthetized with Inactin (thiobutabarbitol, Byk Gulden, Constance, FRG) at 100 mg/kg body wt i.p. and placed on a thermostatically heated table, maintaining rectal temperature at 36–38°C. The trachea was cannulated. Two catheters made from tapered PE-50 tubing were inserted in the left jugular vein for infusions. The left carotid and left femoral arteries were also cannulated for continuous measurement of blood pressure and for sampling blood. An intravenous infusion of 2.5% saline and 0.12% p-aminohippuric acid in normal saline was started at 30 μl·min⁻¹·100 g body wt⁻¹ to maintain euvolemia. To offset the loss of plasma protein as a consequence of surgery, 5% bovine serum albumin (Sigma Chemical Co., St. Louis, Mo.) in normal saline was intravenously infused at 27 μl·min⁻¹·100 g body wt⁻¹ during the surgical period only. The right ureter was also cannulated. The left kidney was carefully isolated from perirenal tissue, and the left papilla was exposed by excising the ureter. The catheter attached to the implanted matrix was flushed with 20 μl saline, and pressure was recorded using a transducer calibrated between 0 and 20 mm Hg. The kidney was placed in a Lucite holder containing cotton saturated in mineral oil and covered with plastic cling wrap to prevent drying. Care was taken not to stretch the renal artery or vein. For vasa recta recordings, the cling wrap was temporarily removed. A Blalock clamp placed around the renal aorta above the renal arteries allowed for adjustment of the RPP. After the acute experiment, all animals were killed by air embolism while still under deep anesthesia, and the kidneys were removed and weighed.

Fluorescence Videomicroscopy

The technique for determination of QVR has been described previously. Briefly, 0.25 ml fluorescein isothiocyanate-labeled γ-globulin was injected intravenously at the end of the stabilization period. The papilla was positioned under the objective of an epifluorescence microscope (Leitz, Wetzlar, FRG) and illuminated with fluorescent light, and the image was transmitted to a low light–sensitive television camera (Newvision 70-C, Dage-MTI, Inc., Michigan City, Ind.), displayed on a high-resolution television monitor, and recorded on videotape. Two areas near the base of the exposed papilla were recorded during each experimental period. The diameter of each vasa recta was measured with a caliper on stopped-frame images projected onto the television monitor and corrected for the final magnification of the monitor image (×1,000). Erythrocyte velocity (VRBC) was measured by a dual-slit cross-correlation technique from the videotape recordings. Velocities were analyzed with a video photometric analyzer, a personal computer (P/S2 model 30, IBM), and software (model 204C, Instruments for Physiology & Medicine, Inc., San Diego, Calif.). The manufacturer’s velocity tracking system calibration was validated with a smear of red blood cells on a rotating wheel. QVR was calculated from cross-sectional area and average blood velocity (Vblood) as follows:

\[ Q_{VR} = V_{blood} \cdot \pi \cdot D^{2}/4 \]

where D is the diameter of a vasa rectum and Vblood is the cross-sectional blood velocity. VRBC was converted to Vblood by an equation derived empirically from studies of the relation between VRBC and Vblood in quartz capillary tubes. In each experiment, two to five ascending vasa recta and one to three descending vasa recta were measured in both periods. Each capillary served as its own control. These separate measurements in each rat were averaged for each period. The averages are then the individual data used for determination of means and standard errors in each group.

Experimental Groups

Five groups of animals were studied. They are described below.

Intact renal capsule group (n=12). In this group, the effect of increasing RPP on QVR, RIHP, and renal excretory function was examined in rats with encapsulated kidneys. At the end of surgery, RPP was set at 100 mm Hg. Rats were then allowed 1 hour to recover after completion of the surgical procedure. A clearance period (30 minutes) from the right kidney was started, during which mean arterial pressure, RPP, and RIHP were measured with pressure transducers and recorded at 5-minute intervals. Midway through the clearance period, 140 μl blood was withdrawn for p-aminohippuric acid and inulin measurements. QVR was recorded for 2 minutes in each of two areas on the papilla. After the first clearance period, RPP was set at a higher level by releasing the aortic clamp. Thirty minutes later, a second clearance and videomicroscopy recording were performed. The reported RPP and RIHP are the averages of the recordings throughout each clearance period.

Decapsulation group (n=12). In this group, the effect of increasing RPP on QVR, RIHP, and renal excretory function was examined in rats in which acute bilateral renal decapsulation was carefully performed. Otherwise, the surgery and protocol were identical to the procedure in the intact capsule group.

Time control decapsulated group (n=7). The protocol, including surgery, clearance periods, and the video recordings, was identical in design to the protocol in the decapsulated group except that RPP was set at 100 mm Hg throughout the experiment.
TABLE 1. Effect of Changes in Renal Perfusion Pressure on Kidney Function

<table>
<thead>
<tr>
<th>Group</th>
<th>RPP (mm Hg)</th>
<th>RIHP (mm Hg)</th>
<th>C_in (ml · min⁻¹ · gKwt⁻¹)</th>
<th>C_PAH (ml · min⁻¹ · gKwt⁻¹)</th>
<th>V (µl · min⁻¹ · gKwt⁻¹)</th>
<th>UNaV (µeq · min⁻¹ · gKwt⁻¹)</th>
<th>FENa (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ENCAP (n=12)</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Low RPP</td>
<td>101±0.3</td>
<td>4.6±1.3</td>
<td>0.82±0.07</td>
<td>2.0±0.3</td>
<td>16±3</td>
<td>2.10±0.38</td>
<td>1.67±0.24</td>
</tr>
<tr>
<td>High RPP</td>
<td>132±2.9*</td>
<td>7.6±1.3†</td>
<td>0.86±0.13</td>
<td>2.4±0.3</td>
<td>20±3‡</td>
<td>3.36±0.62*</td>
<td>2.46±0.39‡</td>
</tr>
<tr>
<td><strong>DECAP (n=12)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Low RPP</td>
<td>100±0.3</td>
<td>4.0±0.6</td>
<td>0.71±0.08</td>
<td>1.9±0.2</td>
<td>13±2</td>
<td>1.76±0.28</td>
<td>1.80±0.35</td>
</tr>
<tr>
<td>High RPP</td>
<td>134±2.2*</td>
<td>3.6±0.6§</td>
<td>0.85±0.09</td>
<td>2.1±0.3</td>
<td>14±2</td>
<td>2.12±0.31†</td>
<td>1.86±0.37</td>
</tr>
<tr>
<td><strong>Time control (n=7)</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Low RPP</td>
<td>100±0.0</td>
<td>3.1±0.6</td>
<td>0.91±0.13</td>
<td>2.3±0.5</td>
<td>12±3</td>
<td>1.22±0.35</td>
<td>1.10±0.43</td>
</tr>
<tr>
<td>Low RPP</td>
<td>100±0.0‡</td>
<td>3.0±0.7</td>
<td>0.90±0.16</td>
<td>2.1±0.4</td>
<td>12±2</td>
<td>1.09±0.31</td>
<td>0.97±0.33</td>
</tr>
</tbody>
</table>

RPP, renal perfusion pressure; RIHP, renal interstitial hydrostatic pressure; C_in, inulin clearance; C_PAH, p-aminohippuric acid clearance; V, urine flow; UNaV, urinary excretion of sodium; FENa, fractional excretion of sodium; gKwt, grams kidney weight; ENCAP, intact capsule group; n, number of rats; DECAP, decapsulated group; time control, time control decapsulated group. Values are mean±SEM.

* p<0.01, † p<0.001, § p<0.05 vs. corresponding value for low RPP periods.
‡ p<0.05 vs. corresponding period for ENCAP.
§ p<0.05 vs. corresponding period for DECAP.

Ureteral excision group (n=4). Because RIHP was measured in the left kidney, in which the ureter was excised to permit visualization of papillary vasa recta, it was possible that the ureteral excision itself changed RIHP. Therefore, the effect of exposing the papilla by ureteral excision on RIHP was determined in this group. After equilibration from surgery, RIHP in the excised left kidney was measured for 20 minutes before and after ureteral excision. This experiment was performed both at low RPP (100 mm Hg) and high RPP (140 mm Hg).

Bilateral renal response group (n=6). Because measurement of Qvr necessitated exposure of the left papilla, it was possible that the response was different in the left kidney compared with the right kidney with an intact ureter. Rats in this group were studied to assess whether the renal response of the right kidney to an increase in RPP occurred similarly in the left kidney. The protocol was similar to that in the first three groups, except Qvr was not measured. Instead, urine was collected directly from the exposed papilla of the left kidney over a 5–10-minute period with a smooth-tipped 100-µl glass capillary tube that was gently slipped over the tip of the papilla as previously described.18 Urine was also collected separately over a similar period from the contralateral kidney by use of the ureteral catheter.

Analyses

Inulin concentrations in plasma and urine were determined by the anthrone method.19 p-Aminohippuric acid was detected chemically according to Smith et al.20 Plasma and urine sodium concentrations were determined by flame photometer (model E-2A, Beckman Instruments Inc., Brea, Calif.).

Statistics

All values are expressed as mean±SEM. Comparisons were made with a paired or unpaired Student’s t test (STATVIEW II, Abacus Concepts, Inc., Berkeley, Calif.), as appropriate. Statistical significance was defined as p<0.05.

Results

In all groups studied, body weights were similar and averaged 150±3 g. The effects on RIHP and renal excretory function of allowing RPP to increase from 100±0.5 to 132±2.9 or 134±2.2 mm Hg in the intact renal capsule and decapsulated groups, respectively, and of keeping RPP constant at 100 mm Hg in the time control group are summarized in Table 1. In animals with encapsulated kidneys, increases in RPP were associated with significant increases in RIHP, urine flow, UNaV, and fractional excretion of sodium (FENa). Acute bilateral renal decapsulation prevented the increase in RIHP associated with elevations in RPP and also abolished both pressure-natriuretic and pressure-diuretic responses. The difference in UNaV from low RPP to high RPP was significantly greater in the encapsulated group compared with the decapsulated group (1.26±0.30 versus 0.36±0.27 µeq · min⁻¹ · g kidney wt⁻¹, respectively; p<0.05); and the change in UNaV relative to the change in RPP (ΔUNaV/ΔRPP) was significantly greater in encapsulated animals (0.040±0.009 µeq · min⁻¹ · g kidney wt⁻¹ · mm Hg⁻¹) compared with decapsulated animals (0.009±0.009 µeq · min⁻¹ · g kidney wt⁻¹ · mm Hg⁻¹, p=0.01). Similarly, FENa did not change significantly (1.80–1.86%) in the decapsulated group as RPP was allowed to change from 100 to 134 mm Hg. No significant changes in RIHP, urine flow, UNaV, and FENa occurred between periods in the time control decapsulated group of rats in which RPP was maintained at 100 mm Hg. RIHP and renal excretory function in the time control group were not significantly different from those values in the decapsulated group of rats at low RPP (100 mm Hg). In all three groups, no significant differences in inulin and p-aminohippuric acid clearances were observed between low and high RPP periods.

The effect of RPP on V_RBC, vasa recta diameter, and Qvr is shown in Table 2. The average capillary diameter did not change between periods of low and high RPP, and accordingly, changes in Qvr paralleled those in V_RBC. Qvr in both descending and ascending vasa recta increased significantly and to a similar extent as RPP was allowed to increase in the presence and absence of an intact renal capsule. When RPP was held constant at 100 mm Hg, vasa recta diameter, V_RBC, and thus Qvr did not change significantly in either ascending or descending vasa recta throughout both periods. The percent change in Qvr is depicted in Figure 1. Descending vasa
TABLE 2. Effect of Changes in Renal Perfusion Pressure on Vasa Recta Hemodynamics

<table>
<thead>
<tr>
<th>Group</th>
<th>$n$</th>
<th>$V_{\text{RB}}$ (mm/sec)</th>
<th>Diameter (µm)</th>
<th>$Q_{\text{VR}}$ (nl/min)</th>
<th>$n$</th>
<th>$V_{\text{RB}}$ (mm/sec)</th>
<th>Diameter (µm)</th>
<th>$Q_{\text{VR}}$ (nl/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENCAP (N=12)</td>
<td></td>
<td>0.53±0.05</td>
<td>16.5±1.2</td>
<td>4.71±0.89</td>
<td>54</td>
<td>0.33±0.02</td>
<td>18.0±0.5</td>
<td>2.76±0.23</td>
</tr>
<tr>
<td>Low RPP</td>
<td>30</td>
<td>0.59±0.05*</td>
<td>16.6±1.2</td>
<td>5.52±0.92*</td>
<td>54</td>
<td>0.39±0.02*</td>
<td>17.9±0.5</td>
<td>3.48±0.24*</td>
</tr>
<tr>
<td>High RPP</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td>53</td>
<td>0.30±0.01</td>
<td>18.2±0.7</td>
<td>2.55±0.31</td>
</tr>
<tr>
<td>DECAP (N=12)</td>
<td></td>
<td>0.56±0.02</td>
<td>15.5±0.8</td>
<td>4.44±0.49</td>
<td>53</td>
<td>0.36±0.01*</td>
<td>18.3±0.7</td>
<td>3.33±0.33*</td>
</tr>
<tr>
<td>Low RPP</td>
<td>32</td>
<td>0.62±0.03†</td>
<td>15.7±0.7</td>
<td>5.12±0.53†</td>
<td>22</td>
<td>0.35±0.02</td>
<td>15.6±0.6</td>
<td>2.31±0.19</td>
</tr>
<tr>
<td>High RPP</td>
<td>32</td>
<td></td>
<td></td>
<td></td>
<td>22</td>
<td>0.34±0.03</td>
<td>15.6±0.6</td>
<td>2.10±0.25</td>
</tr>
</tbody>
</table>

DVR, descending vasa recta; AVR, ascending vasa recta; $n$, number of vessels; $V_{\text{RB}}$, vasa recta red blood cell velocity; $Q_{\text{VR}}$, vasa recta blood flow; ENCAP, intact capsule group; N, number of animals; DECAP, decapsulated group; time control, time control decapsulated group. Values are mean±SEM.

*p<0.001, †p<0.01 vs. low RPP period for same group.

recta blood flow increased by 20.2±7.0% in the decapsulated group, an increase similar to the increase in the intact capsule group (23.6±5.7%) and significantly greater than the increase in the time control group (0.80±4.2%). Similar changes were observed in ascending vasa recta blood flow, with blood flow increasing by 36.4±8.7% in the decapsulated group and 29.3±7.5% in the intact capsule group and decreasing by 9.4±6.4% in the time control group.

In the ureteral excision group, RIHP was not different before (6.7±2.7 mm Hg) and after (6.9±2.9 mm Hg) ureteral excision. The lack of effect of ureteral excision on RIHP was observed in all rats studied and was independent of the prevailing RPP.

In the last group (bilateral renal response group), urine flow and $U_{\text{Na}}\text{V}$ responses were not significantly different in the right (ureteral catheter) and left (exposed papilla) kidneys. At an RPP of 100 mm Hg, urine flow and $U_{\text{Na}}\text{V}$ were similar in both kidneys (urine flow, 6.3±2.7 µl/min on the right versus 10.3±5.7 µl/min on the left; $U_{\text{Na}}\text{V}$, 1.09±0.59 µeq/min on the right versus 0.53±0.26 µeq/min on the left). After RPP was allowed to increase to 133±2.0 mm Hg, urine flow increased to 8.8±3.3 and 13.1±5.5 µl/min in the right and left kidneys, respectively. Similarly, $U_{\text{Na}}\text{V}$ increased to 1.47±0.76 and 1.68±0.98 µeq/min in the right and left kidneys, respectively.

Discussion

The results of the present study demonstrate that an elevation in RPP causes a significant increase in $Q_{\text{VR}}$, both in the presence and absence of a rise in RIHP. By dissociating the increase in $Q_{\text{VR}}$ from the increase in RIHP and $U_{\text{Na}}\text{V}$ by means of acute renal decapsulation, the present study also indicates that for an increase in $Q_{\text{VR}}$ to play a role in pressure natriuresis it must do so in association with an increase in RIHP.

Implicit to the hypothesis that changes in inner medullary blood flow are linked causally to the pressure natriuretic response is a lack of efficient autoregulation in this microcirculatory region. Conflicting data, however, exist in the literature regarding the autoregulation of medullary blood flow. Studies have reported evidence both for autoregulation and against efficient medullary autoregulation. Using the videomicroscopic technique, Cohen et al. reported that $V_{\text{RB}}$ of medullary vasa recta was unaltered over the pressure range of 85–125 mm Hg, although it increased significantly at higher pressures. On the other hand, using both laser Doppler and videomicroscopic techniques, Roman et al. showed that papillary blood flow in volume-expanded hormonally clamped rats varied directly with RPP over a wide range of pressures. It was also observed in the latter study that vasa recta capillary pressures rose in parallel with RPP. This is in close agreement with the present study, in which consistent and significant increases in

![FIGURE 1. Bar graph showing effect of renal perfusion pressure on the percent change in vasa recta blood flow (%CHANGE QVR). Renal perfusion pressure increased from 101±0.4 to 132±2.9 mm Hg in rats with intact kidney capsule (ENCAP) and from 100±0.3 to 134±2.2 mm Hg in rats with decapsulated kidney (DECAP). Renal perfusion pressure was kept at 100±0.0 mm Hg in time control decapsulated rats (TIME CON). QVR in decreasing (DVR) and ascending (AVR) vasa recta increased significantly with increases in renal perfusion pressure in ENCAP and DECAP groups (see also Table 2). †p<0.05 vs. corresponding value for DECAP.](http://circres.ahajournals.org/content/71/5/1156/F1.large.jpg)
QVR were observed as RPP was allowed to increase, despite autoregulation of whole-kidney renal blood flow and glomerular filtration rate. Hydropenic animals seem to exhibit better autoregulation of medullary blood flow than do volume-expanded animals. It is possible that volume expansion inhibits the otherwise efficient tubuloglomerular feedback mechanism that has been shown to operate in the in vitro blood-perfused rat juxtaglomerular nephron preparation. Volume expansion has also been shown to reduce medullary osmolality and to fix the amount of water conserved by the concentrating mechanism, all of which can theoretically affect QVR. Although recruitment of individual vasa recta was not determined in the present study, it is possible that the number of perfused vasa recta capillaries increases with elevations in RPP. If vessel recruitment occurred in the present study, then the blood flow measured in individual vasa recta would actually underestimate the true change in total papillary blood flow with increases in RPP.

Removal of the renal capsule dissociated changes in QVR from RIHP and UNaV; i.e., acute renal decapsulation allowed QVR to increase with increases in RPP but prevented both RIHP and UNaV from increasing. This indicates that the natriuretic response associated with increases in QVR occurs only in the presence of a concomitant rise in RIHP. In the absence of changes in RIHP, an increase in QVR in and of itself is therefore unlikely to be the major mechanism underlying pressure natriuresis. Our studies, in which QVR increased in the decapsulated group but was not associated with an increase in UNaV, suggest that changes in QVR do not significantly alter UNaV.

It is also possible that increases in QVR associated with a rise in RPP occur secondary to the rise in urine flow in the collecting tubule. An increase in tubular fluid flow reaching the papillary collecting ducts during water diuresis has been shown to increase absolute net water flux into the papilla compared with the antidiuretic state. Because there are no lymphatics in the papilla, all reabsorbed fluid must be removed by the vasa recta to maintain mass balance, thereby elevating blood flow in the inner medulla. This explanation, however, is not supported by the finding in the decapsulated group of rats, in which a rise in QVR developed despite no change in urine flow. Similarly, the rise in QVR cannot be due to changes in RIHP, since QVR increased without a change in RIHP in this same group of animals. It is likely, therefore, that increases in RPP directly increase QVR.

This study is concerned with the principal intrarenal hemodynamic factors postulated to play a role in the pressure natriuresis response, i.e., QVR and RIHP. Hormonal, autocrine, and paracrine factors likely impact on these two factors, thereby modulating the pressure natriuretic response. For example, intrarenal angiotensin II, prostaglandins, endothelium-derived relaxing factor, and endothelin may alter the tone in juxtamedullary efferent arterioles or vasa recta to change QVR and pressure. Prostaglandins may also alter the effect of increases in RIHP to diminish sodium reabsorption.

The present study supports the thesis that RIHP plays a central role in regulating UNaV during elevations in RPP. It confirms that renal decapsulation prevents the increase in RIHP and blunts the associated natriuresis. Further, it indicates that the blunting effect of renal decapsulation on RIHP is not due to a lack of increases in QVR when RPP is raised. A more likely explanation is that renal decapsulation alters the functional compliance characteristics of the renal interstitium in such a way as to prevent increases in vasa recta hydrostatic pressure from contributing, directly or indirectly, to the rise in RIHP normally evident in pressure natriuresis. The mechanism whereby increases in RIHP reduce the net tubular reabsorption of sodium and water remains to be established. One theory proposes an effect of interstitial pressure to enhance the rate of passive paracellular back leak of ions across the proximal tubular epithelium. Another possibility is that increases in interstitial pressure may cause the release of prostaglandins or other paracrine substances from renal interstitial cells, which would in turn act directly or indirectly on renal tubular epithelial cells to alter transport of solute and water. In this regard, Pawlowska et al have shown that prostaglandin blockade blunts the natriuresis associated with direct increases in RIHP.

In summary, pressure natriuresis in the rat was associated with increases in both QVR and RIHP. Acute renal decapsulation abolished the increase in RIHP and
pressure natriuresis and diuresis but did not affect the increase in \( Q_{VR} \). It is concluded that an elevation in RPP increases \( Q_{VR} \), which results in natriuresis only in association with an increase in RIHP.

Acknowledgments

The authors would like to thank John A. Haas and Marcy Ongstad for technical assistance, June M. Hanke for secretarial assistance, and Franklyn G. Knox for his invaluable advice.

References

Relation between vasa recta blood flow and renal interstitial hydrostatic pressure during pressure natriuresis.
E Farrugia, J C Lockhart and T S Larson

doi: 10.1161/01.RES.71.5.1153

*Circulation Research* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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