Luminal volume and reabsorption in the loop of Henle: Effects of blood pressure and noradrenalin

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Luminal volume and reabsorption in loop of Henle: Effects of blood pressure and noradrenalin. These experiments examine the interrelationships of luminal volume (V) and reabsorption (R) in the loop of Henle and arterial pressure (P). Re-collection micro-puncture techniques were used to obtain samples from late proximal and early distal tubules before and after acute alteration of P in diuretic rats. In group 1, P was decreased from 140 ± 2 to 113 ± 3 mm Hg with a servocontrolled aortic clamp between the renal arteries; flow into the loop (Q) decreased from 21.8 ± 0.8 to 16.9 ± 1.0 nI/min; Vr, estimated from mean flow through the loop and transit time, decreased from 6.0 ± 0.3 to 5.1 ± 0.3 nl; Vr, estimated from resistance to flow, also decreased from 3.5 to 2.8 nl; R decreased from 10.6 ± 0.5 to 9.4 ± 0.5 nI/min. In group 2, P increased from 121 ± 3 to 142 ± 3 mm Hg with norepinephrine infusion (2 to 4 μg/kg-min). Q increased from 16.6 ± 0.7 to 22.5 ± 1.4 nI/min; Vr was unchanged; and R increased from 9.4 ± 0.6 to 11.4 ± 1.1 nI/min. In group 3, when P was held constant with the aortic clamp, norepinephrine infusion decreased Q from 24.4 ± 0.9 to 20.3 ± 1.4 nI/min, left R unaltered, but decreased Vr from 7.9 ± 0.3 to 5.5 ± 0.4 nl. R did not correlate significantly with V in any group. Conclusion. Norepinephrine decreases Vr in the loop of Henle; Vr does not appear to be a determinant of R from Henle’s loop in these acute experiments. Acute variations of arterial pressure do not produce the correlations between R and Vr observed in chronically hypotensive and hypertensive animals.

Volume luminal et réabsorption dans l’anse de Henle: Effets de la pression artérielle et de la noradrenaline. Ces expériences étudient les relations de la pression artérielle (P) du volume luminal de l’anse de Henle (V) et de la réabsorption (R) dans l’anse de Henle. La technique des microponctions avec recollection a été employée pour obtenir des échantillons de fin de tube proximal et de début de tube distal avant et après une modification aiguë de P chez des rats en état de diurèse. Dans le groupe 1, P a été diminuée de 140 ± 2 à 113 ± 3 mm Hg au moyen d’un clamp aortique à contrôle asservi placé entre les artères rénales. Le débit dans l’anse (Q) a diminué de 21.8 ± 0.8 à 16.9 ± 1.0 nI/min. Vr, calculée à partir du débit moyen dans l’anse et du temps de transit, a diminué de 6.0 ± 0.3 à 5.1 ± 0.3 nl; Vr, calculée à partir de la résistance au flux a aussi diminué de 3.5 à 2.8 nl; R a diminué de 10.6 ± 0.5 à 9.4 ± 0.5 nI/min. Dans le groupe 2, P a été augmentée de 121 ± 3 à 142 ± 3 mm Hg par une perfusion de norépinephrine de 2 à 4 μg/kg-min. Q a augmenté de 16.6 ± 0.7 à 22.5 ± 1.4 nI/min; Vr n’a pas changé; R a augmenté de 9.4 ± 0.6 à 11.4 ± 1.1 nI/min. Dans le groupe 3, quand P a été maintenue constante au moyen du clamp aortique, la perfusion de norépinephrine a diminué Q de 24.4 ± 0.9 à 20.3 ± 1.4 nI/min. Dans aucun groupe R n’est corrélat significativement à Vr. Conclusion. La norépinephrine diminue Vr dans l’anse de Henle; Vr ne semble pas être un déterminant de la réabsorption dans l’anse de Henle dans ces expériences aiguës. Les variations aiguës de la pression artérielle ne produisent pas les correlations entre R et Vr observées chez les animaux en situation d’hypotension ou d’hypertension chronique.

Relationships between luminal volume and reabsorption as they are jointly affected by changes in blood pressure are examined in this paper. The hypothesis to be tested is that a decrease in blood pressure will lead to an increase in luminal volume of the loop of Henle and an increase in reabsorption, while an increase in blood pressure will produce the opposite effect.

Should such a mechanism relating blood pressure and loop function exist, it would be only one of many factors involved in the pathogenesis of abnormal renal function in edema or hypertension. For example, the effects of arterial pressure on peritubular blood flow and interstitial solute concentrations may outweigh any changes in luminal volume. From our experiments on single loops of Henle performed under conditions which ensure a constant peritubular environment, we conclude, however, that luminal volume, or, more precisely, surface area and thickness of the tubular wall, has a significant effect on reabsorption [1] (Baines et al, submitted for publication). Although this effect is small and therefore may be hard to detect, the cumulative consequences could be appreciable.

Methods

Male Wistar rats, weighing 200 to 300 g, were starved overnight before being anesthetized with i.p. Inactin® (100 mg/kg). Results from two rats in group 1, anesthetized with pentobarbital (Nembutal

Received for publication May 31, 1977; and in revised form March 9, 1978.

0085-2538/78/0014—0255 $01.60 © 1978 by the International Society of Nephrology.
tal®, 50 mg/kg of body wt, i.p.), were indistinguishable from the rest. These are, therefore, not referred to separately. After each rat was placed on a heated animal board, its left kidney was exposed through an incision in the ventral abdominal wall and was immobilized with a semicircular band, which left the hilus untouched. An air curtain incubator (Sage Instruments) kept the exposed area at 37° C. All exposed tissue was covered with Parafilm®. Cannulas (PE-50) were placed in the right jugular vein and advanced towards the right atrium. This cannula was used for injection of 10% lissamine green purified according to the method of Parrehk et al [2].

A C-shaped clamp attached to a servocontrolled pressure regulating device [3] was placed about the aorta between the renal arteries whenever the protocol required regulation of perfusion pressure to the left kidney. The device regulated pressure in the femoral artery to a preset level and held it constant for up to 3 hr. Pressures in femoral and renal arteries were assumed to be equal.

All animals received a priming infusion of isotonic salt solution (sodium, 140 mEq/liter; potassium, 4 mEq/liter; chloride, 119 mEq/liter; and bicarbonate, 25 mEq/liter) at 0.34 ml/min for 10 min followed by a constant infusion at 0.1 ml/min. After a 60-μCi priming injection, 3H-inulin was infused a 3 μCi/min. At least 90 min elapsed between the initial infusion and the start of micropuncture collections.

In preliminary experiments with hydropenic rats, loop function tended to be unstable over the 60 to 90 min of lowered arterial pressure, and the effects of going from high to low pressure appeared to be quantitatively different from those going from low to high pressure. Qualitatively, however, the effects of lowering arterial pressure in hydropenic rats were similar to those reported in this paper for mildly diuretic rats.

*Group 1: Effect of aortic constrictions.* The effect of arterial perfusion pressure on renal function was examined in 12 rats with moderately elevated systemic pressure. One carotid artery was tied off while a thread was placed loosely around the other carotid and its accompanying vagus nerve to raise systemic blood pressure during the initial operative procedure. This maneuver increased the mean arterial pressure to 140 mm Hg and sustained it at this level for at least 3 hr in 9/12 rats. The remaining three rats responded to tightening of the thread around the second carotid artery.

After the blood pressure was raised in this fashion, the servocontrolled clamp was used to reduce femoral artery pressure by approximately 25 mm Hg in six rats. Pressure was kept at this level during the 60- to 90-min equilibration period and the first hour of collection. The clamp was then released, and pressure was allowed to rise for a second set of collections. Pressure was again reduced for a third collection period in two of these rats.

In the other six rats, femoral arterial pressure was allowed to remain high for the first collection period, and then it was lowered by 25 mm Hg for the second set of collections. After we released the aortic constriction so that femoral pressure would increase to the previously high level, a third set of collections was made from two of these rats.

In an additional five rats, tubular pressure was measured with a servonull pressure transducer (P.P.M., San Diego, Calif.) at high and low femoral arterial pressure. In three of these rats, femoral arterial pressure was reduced with the clamp for the first period, then was allowed to rise for a second period, and finally was reduced again for a third set of measurements. In the other two rats, the pressure was high initially, then was lowered, and finally was allowed to rise for the third period.

*Group 2: Effect of norepinephrine.* The effect of norepinephrine-induced rises in pressure was studied by infusing seven rats with 2 to 4 μg/kg-min l-norepinephrine i.v. after an initial control set of urine and tubular fluid collections had been made. A third set of collections was made in three of these rats after the norepinephrine infusion was stopped.

*Group 3: Effect of norepinephrine and aortic constriction.* In a further four rats, aortic constriction was used to prevent the rise in the left renal artery pressure during infusion of 2 to 4 μg/kg-min of l-norepinephrine. As was done with the other two groups, two sets of urine and tubular fluid collections were obtained from this last group.

Micropuncture samples were obtained from late proximal and early distal tubules during the first of the two or three collection periods in each animal. Samples were re-collected from the same tubules after perfusion pressure or norepinephrine infusion was altered. Purified lissamine green [2] injected i.v. was used to locate the collection sites and to measure transit times. Proximal collections were made at less than the tubular fluid flow rate without injecting oil into the tubule.

Volume of micropuncture samples was measured in a calibrated capillary tube. The complete volume of 30 nl or more from proximal samples was transferred to 3.5 ml of water in a counting vial. After 5 to 10 nl was removed for sodium and osmolality
measurements, the remaining distal sample was used for scintillation counting. Tritiated inulin was measured in Aquasol® (New England Nuclear Corp.) in a scintillation counter. Urine and tubular osmolality was measured with a microosmometer (Clifton). Sodium in urine was measured with a flame photometer, (Instrumentation Laboratories), and tubular fluid sodium was measured with a helium glow spectrophotometer (Aminco).

Calculation. Because of potential dead space errors, no urine was collected for 15 min after a change in experimental conditions. Transit times and tubular pressures did not stabilize until 10 to 15 min after conditions were changed; therefore, micropuncture samples were not collected during this transition period.

All estimates of single nephron filtration rate (SNGFR), which are shown in the tables and figures, were made using the results of distal tubular fluid collections. Fluid collections from proximal tubules were incomplete and were made without injecting oil into the tubule to avoid the lodging of droplets in the nephron between collections and to minimize the effect which reducing flow to the distal tubule appears to have on nephron function. Apparent SNGFR was calculated from proximal tubule samples. The proximal tubular fluid sample was accepted only if the apparent SNGFR was less than 50% of the SNGFR calculated from complete distal tubule collections.

Fluid samples from proximal and distal tubules were obtained from different nephrons. Tubular fluid-to-plasma (TF/P) inulin from two to five proximal collections was averaged. This value was used to calculate flow into each loop for which a distal collection had been made. Flow into the loop (QIF) = (individual SNGFR calculated from distal collection) ÷ (average TF/P inulin for all proximal collections in the period). Reabsorption from the loop (R) = QIF - (flow rate in the early distal tubule (QOF)).

Luminal volume was estimated by multiplying the mean flow through the loop × the transit time for that loop. Initially mean flow was calculated as either the arithmetic or geometric mean of QIF and QOF. The results were similar with either estimate. Fluid reabsorption occurs primarily in the first half of the loop and is load-dependent [4, 9, 10]. Therefore, flow in the loop will tend to decrease exponentially at least in the first half of the loop. Because a geometric mean more closely approximates this situation than does an arithmetic mean, the geometric mean was used.

Luminal volumes calculated this way are estimates which indicate only that some part of the loop has dilated or constricted so that the relationship of transit time to flow rate is altered. They are not intended to imply the existence of a homogeneous structure which dilates and constricts uniformly over its entire length.

Statistical significance of results was examined by analysis of variance. Unless otherwise specified, the probabilities indicate rejection of the hypothesis that there is no difference between paired measurements within animals at high and low pressure.

Results

In group 1, initial pressure was low for half of the rats (group 1A); for the other half, initial pressure was high (1B). Urine sodium excretion increased by 5 μEq/min when pressure rose by 22 mm Hg in group 1A and fell by 2 μEq/min when pressure was decreased by 27 mm Hg in group 1B (P < 0.025; paired t test). The only other statistically significant difference was that the fractional water flow in the early distal tubule increased 9% with rising pressure in 1A but fell by 3% when pressure was reduced in 1B (P < 0.025).

There is a tendency for urine flow and fractional excretion to increase with time during micropuncture experiments. This tendency would augment the increment in sodium excretion on going from low pressure to high pressure (group 1A), while it would diminish the decrease in sodium excretion produced by going from high pressure to low pressure (group 1B). As there was no qualitative difference between groups 1A and 1B in the response of load, transit time, and reabsorption to changing pressure, the data were combined for subsequent analysis.

The right ureter as well as the left was cannulated in seven of the group 1 rats. The data are shown in Table 1. Aortic constriction did not significantly affect the function of the right kidney. Inulin clearance, however, decreased significantly in the left kidney (Tables 1 and 2; P < 0.001).

A rise in pressure induced by infusion of norepinephrine was not associated with increased glomerular filtration rate (group 2). Absolute urine flow and sodium excretion increased to the same extent relative to arterial pressure in the left kidneys of groups 1 and 2.

Norepinephrine infusion, when combined with maintenance of a constant arterial pressure (group 3), produced a slight but insignificant decrease of inulin clearance. Despite the constant arterial pres-
sure, urine flow and sodium excretion in group 3 fell to the same extent as they did when arterial pressure was reduced 22 mm Hg by aortic constriction (group 1).

**Nephron function: Group 1.** Tubular pressures were measured only in group 1. Micropuncture samples were not collected from the rats used for pressure measurements. As can be seen from Table 3, renal function in this subgroup of eight paired observation periods in five rats was indistinguishable from that in the larger group used for collecting micropuncture samples (Table 2). Therefore, the micropressure measurements in the smaller group can be assumed to represent those that would have been found in the larger group if their pressures had been measured.

Mean values for micropuncture samples are given in Table 4. When arterial pressure was lowered by aortic constriction in group 1, SNGFR decreased (*P* < 0.001). Absolute reabsorption from proximal tubules was unchanged, but fractional reabsorption increased (*P* < 0.05). Delivery of fluid to the loop decreased (*P* < 0.001), as did reabsorption from the loop (*P* < 0.01). Estimated luminal volume decreased 18% (*P* < 0.001).

**Group 2.** When pressure was increased by nor-epinephrine, SNGFR rose absolutely (*P* < 0.001, Table 4) and relative to total kidney filtration rate; \( C_{in}/\text{SNGFR} \) was 38.1 ± 1.5 and 33.6 ± 1.1 at high and low pressures, respectively (*P* < 0.001). Absolute reabsorption from the proximal tubule did not change, but fractional reabsorption did decrease (*P* < 0.05). Load delivered to the loop (*P* < 0.001) and reabsorption in the loop (*P* < 0.01) increased. In contrast to the results found in group 1, estimated luminal volume was 9% greater at low than at high arterial pressure, but the difference was not significant (*P* < 0.1).

**Group 3.** When arterial perfusion pressure to the kidney was kept constant, norepinephrine infusion decreased SNGFR (*P* < 0.001). Load to the loop decreased (*P* < 0.01), but reabsorption did not change. There was a 30% decrease in estimated luminal volume of the loop (*P* < 0.01).

**Discussion**

Observations of loop function in both hypertensive animals and edematous animals suggest a causal connection between arterial pressure, transit time

<table>
<thead>
<tr>
<th>Blood pressure mmHg</th>
<th>Urine flow µL/min</th>
<th>Urine sodium mEq/liter</th>
<th>Urine osmolality mOsm/kg</th>
<th>( C_{in} ) ml/min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Group 1: Effect of aortic constriction (N = 16)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constriction</td>
<td>112 ± 2</td>
<td>27 ± 2</td>
<td>221 ± 14</td>
<td>1,028 ± 56</td>
</tr>
<tr>
<td>No Constriction</td>
<td>140 ± 2</td>
<td>9 ± 2</td>
<td>212 ± 22</td>
<td>714 ± 55</td>
</tr>
<tr>
<td><strong>Group 2: Effect of 2 to 7 µg/kg/min of 1-norepinephrine (N = 9)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>121 ± 3</td>
<td>23 ± 3</td>
<td>189 ± 19</td>
<td>705 ± 95</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>142 ± 3</td>
<td>49 ± 5</td>
<td>176 ± 24</td>
<td>522 ± 23</td>
</tr>
<tr>
<td><strong>Group 3: Effect of 2 to 4 µg/kg/min of 1-norepinephrine with aortic constriction (N = 4)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>125 ± 4</td>
<td>27 ± 4</td>
<td>172 ± 17</td>
<td>703 ± 88</td>
</tr>
<tr>
<td>Norepinephrine &amp; constriction</td>
<td>125 ± 3</td>
<td>8 ± 1</td>
<td>212 ± 15</td>
<td>1,022 ± 172</td>
</tr>
</tbody>
</table>

\(^{a}\) Values are means ± SEM. \( C_{in} \) means inulin clearance.

\(^{b}\) *P* < 0.05.

\(^{c}\) *P* < 0.01.

\(^{d}\) *P* < 0.001.

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**Table 1. Left and right kidney function in seven rats with aortic constriction**

<table>
<thead>
<tr>
<th></th>
<th>Urine flow µL/min</th>
<th>Inulin clearance mL/min</th>
<th>Sodium excretion µEq/min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low pressure</td>
<td>High pressure</td>
<td>Low pressure</td>
</tr>
<tr>
<td>Left kidney</td>
<td>9 ± 2</td>
<td>28 ± 6</td>
<td>1.07 ± 0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.0 ± 0.4</td>
</tr>
<tr>
<td>Right kidney</td>
<td>24 ± 3b</td>
<td>23 ± 3</td>
<td>1.32 ± 0.09b</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.3 ± 0.8a</td>
</tr>
</tbody>
</table>

\(^{a}\) *P* < 0.01.

\(^{b}\) *P* < 0.001.
in Henle’s loop, and reabsorption. On the one hand, in rats, chronic hypertension was associated with decreased transit time and reabsorption in Henle’s loop [4]. These shortened transit times can be explained by assuming decreased volume in Henle’s loop [4]. On the other hand, chronic hypotension accompanying congestive failure due to arteriovenous fistulae in rats [5] and vena caval constriction in dogs [6], was associated with increased transit time and reabsorption. An increase in overall or effective luminal volume of the loop would account for the prolonged transit times. Thus, it appears that low arterial pressure may be associated with increased luminal volume and high arterial pressure with reduced luminal volume in Henle’s loop.

In a collapsible tube such as Henle’s loop, luminal volume is determined by flow, entry and exit pressures, peritubular pressure, and wall compliance [7]. An increase in arterial pressure could bring about a rise in peritubular pressure [8, 9] which collapses the loop. Low arterial pressure could produce the reverse effect.

Lumen volume may relate to reabsorption in at least two ways. First, hydrostatic pressure which influences lumen volume may also drive fluid flow across the wall [10]. Second, surface area and thickness of the wall, which vary with luminal volume, may determine permeability per unit length. Schnermann [11] suggested that transit or contact time, which increases with lumen volume, influences reabsorption; we have shown by mathematical analysis and computer simulation, however, that contact time alone does not influence reabsorption in the loop [12].

The experiments described in this paper were designed to examine the correlation between estimated luminal volume and reabsorption in Henle’s loop when arterial pressure was changed acutely.

The complex nature of Henle’s loop makes only qualitative estimates of luminal volume possible. When flow rate along a tube is constant, luminal volume can be calculated from the product of transit time and flow. When fluid is absorbed in the tube, the situation, however, is more complicated. Two extremes can be postulated: either all the fluid absorption occurs adjacent to the entrance, or all

Table 3. Effect of arterial blood pressure on intrarenal pressures

<table>
<thead>
<tr>
<th>Blood pressure mm Hg</th>
<th>Proximal pressure mm Hg</th>
<th>Distal pressure mm Hg</th>
<th>Capillary pressure mm Hg</th>
<th>C/in ml/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>109 ± 4</td>
<td>11.0 ± 0.9</td>
<td>6.5 ± 0.5</td>
<td>6.2 ± 0.4</td>
<td>1.14 ± 0.04</td>
</tr>
<tr>
<td>136 ± 6</td>
<td>13.2 ± 1.0</td>
<td>8.5 ± 0.8</td>
<td>7.5 ± 0.8</td>
<td>1.32 ± 0.05</td>
</tr>
</tbody>
</table>

a Values are means ± SEM. C/in means inulin clearance.
b P < 0.05.
c P < 0.01.
d P < 0.001.

Table 4. Micropuncture data

<table>
<thead>
<tr>
<th>Arterial pressure mm Hg</th>
<th>SNGFR nI/min</th>
<th>TFP/P inulin</th>
<th>Transit time, sec</th>
<th>Distal fluid Na mEq/liter</th>
<th>Load to loop mOsm/kg</th>
<th>Reabsorption from loop nI/min</th>
<th>Loop “volume” µl</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td></td>
<td>Proximal</td>
<td>Distal</td>
<td>Proximal</td>
<td>Distal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Group 1: Effect of aortic constriction

Constriction 112 ± 2 34.5 ± 1.2 2.16 ± 0.06 5.94 ± 0.70 9.2 ± 0.5 29.6 ± 1.8 63 ± 14 144 ± 9 16.9 ± 1.0 9.4 ± 0.5 5.1 ± 0.3

No constriction 140 ± 2 39.2 ± 1.2 1.88 ± 0.06 3.95 ± 0.36 8.3 ± 0.3 24.0 ± 0.9 62 ± 16 145 ± 6 21.8 ± 0.8 10.6 ± 0.5 6.0 ± 0.3

Group 2: Effect of 2 to 4 µg/kg · min of l-norepinephrine

Control 121 ± 3 29.9 ± 1.3 1.83 ± 0.08 4.45 ± 0.30 8.4 ± 0.2 30.7 ± 2.9 75 ± 19 132 ± 22.5 ± 1.4 11.4 ± 1.1 4.8 ± 0.3

Norepinephrine 142 ± 3 34.9 ± 1.5 1.62 ± 0.07 3.36 ± 0.18 6.9 ± 1.0 18.9 ± 1.1 84 ± 19 132 ± 22.5 ± 1.4 11.4 ± 1.1 4.8 ± 0.3

Group 3: Effect of 2 to 4 µg/kg · min of l-norepinephrine with aortic constriction

Control 125 ± 4 42.0 ± 1.4 1.73 ± 0.07 3.81 ± 0.21 8.1 ± 0.21 25.3 ± 0.9 — 99 ± 6 24.4 ± 0.9 13.0 ± 0.7 7.9 ± 0.3

Norepinephrine & constriction 125 ± 3 35.9 ± 2.3 1.72 ± 0.04 4.69 ± 0.32 7.7 ± 0.27 26.8 ± 0.2 — 114 ± 8 20.3 ± 1.4 12.6 ± 1.3 5.5 ± 0.4

a Values are mean ± SEM.
b P < 0.05.
c P < 0.01.
d P < 0.001.
the fluid is absorbed immediately adjacent to the exit. In the first case, flow along the tube is equal to outflow as soon as the short absorbing segment at the entrance is passed. Volume of the lumen is correctly calculated as outflow times transit time. In the second case, flow along the tube up to the exit is equal to inflow; here luminal volume is calculated correctly as inflow times transit time. Theoretically it would be possible to shift from one pattern to the other, while inflow, outflow, and transit time remain constant. Under one pattern of absorption outflow times transit time would correctly represent the luminal volume; under the other, outflow times transit time would give the correct answer.

If, however, absorption is distributed along the length of the tube and if the magnitude may vary but not the pattern (i.e., distribution), then we can assume that a change in the product of transit time and mean flow indicates a parallel change in luminal volume.

There is no reason to believe that reduction of arterial pressure or norepinephrine infusion altered the distribution or pattern of fluid absorption along Henle’s loop. I assume, therefore, that changes in luminal volume can be estimated from changes in the product of mean flow and transit time.

To differentiate correlations of reabsorption with load from correlations with volume, I used multiple variable regression analysis with reabsorption as the dependent variable (BMD P2R programme, Biomedical Computer Programme, University of California Press, 1975). The results are shown in Table 5.

In group 1, arterial pressure was lowered with minimal disruption of extrarenal hormonal and nervous factors which might influence kidney function. That this was achieved is shown by the absence of change in right kidney function while arterial pressure to the left kidney was lowered (Table 1).

When arterial pressure was lowered and both load and reabsorption from the loop decreased (P < 0.001 and P < 0.01), calculated volume of the loop also decreased (P < 0.001). The estimated change in

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Load*</th>
<th>Volume*</th>
<th>Pressure*</th>
</tr>
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<tbody>
<tr>
<td>Volume (L/H)</td>
<td>0.534</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressure (L/H)</td>
<td>0.130</td>
<td>-0.196</td>
<td></td>
</tr>
<tr>
<td>Reabsorption (L/H)b</td>
<td>0.438</td>
<td>0.161</td>
<td>0.152</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume (L/H)</td>
<td>0.280</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressure (L/H)</td>
<td>0.671</td>
<td>0.348</td>
<td></td>
</tr>
<tr>
<td>Reabsorption (L/H)b</td>
<td>0.049</td>
<td>-0.271</td>
<td>0.201</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume (C/N)</td>
<td>0.677</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressure (C/N)</td>
<td>-0.021</td>
<td>-0.162</td>
<td></td>
</tr>
<tr>
<td>Reabsorption (C/N)b</td>
<td>0.452</td>
<td>0.320</td>
<td>-0.587</td>
</tr>
</tbody>
</table>

* For groups 1 and 2, values at low pressure (L) are divided by values at high pressure (H). For group 3, values from control period (C) are divided by values obtained during norepinephrine infusion with aortic constriction (N).

b Results of stepwise multiple variable regression analysis: Reabsorption (L/H) = 1.2 ± 0.4 × load (L/H) - 0.009; P < 0.01.

c No significant correlation with reabsorption (L/H).

d Results of stepwise multiple variable regression analysis: Reabsorption (C/N) = -4.8 ± 2.1 × pressure (C/N) - 6.7; P < 0.05.

The decrease in hydrostatic pressure from proximal to distal tubule was 5.4 mm Hg at low pressures and 4.7 mm Hg at high pressures (Table 3). Thus, resistance to flow was less at the higher arterial pressures. Luminal volumes for single loops of Henle, calculated with Poiseuille’s equation, were 2.8 nl at low pressures and 3.5 nl at high pressures, a difference of 0.7 nl. Estimates, based on transit time, of the difference between luminal volumes at low and high pressures yielded a similar result, 0.9 nl. Therefore, it is likely that luminal volume decreased primarily in the resistance segment. This is usually assumed to be the thin descending limb [11] and possibly the thick ascending limb [7].

When arterial pressure was lowered in group 1, load delivered to the loop decreased. This probably caused the luminal volume to decrease. This conclusion comes from a comparison of group 1 with experiments in which the loop was microperfused at different rates in rats with constant blood pressure. In microperfused loops, luminal volume decreases as perfusion rate is reduced [5, 7]. Reabsorption rate also decreased with perfusion rate [5, 17]. The

\begin{equation}
\text{Luminal volume} = \pi r^2 L, \quad r^2 = \sqrt{\pi/8 \times Q \times L \times \eta/(P_P - P_D)},
\end{equation}

where \(L\) is mean flow (cm\(^2\) \cdot sec\(^{-1}\)), \(L = 1.2\) cm, and \(\eta = 7 \times 10^{-9}\) poise, where \(P_P\) is the proximal pressure and \(P_D\) is the distal pressure.

In incomplete autoregulation of GFR (Tables 1 and 2) may have been due to the mild saline diuresis. A similar response appears in the work of Kunau and Lameire [13] who observed a 17% increase in GFR when they raised blood pressure from 122 to 169 mm Hg by carotid occlusion and vagotomy in six saline diuretic rats. In their experiments, the increase was not statistically significant (P < 0.1), possibly because of the small number of animals studied. Hydropenic animals appear to autoregulate GFR more efficiently than do saline diuretic animals [14, 15]; this, however, is not always the case [16].
same relationships were found in group 1 experiments; that is with a reduced load to the loops, luminal volume and reabsorption decreased (Table 5). Relationships among load, reabsorption, and volume in group 1 were quantitatively very similar to those observed in microperfusion experiments. It appears, therefore, that an acute reduction in blood pressure decreased flow into the loop without affecting the relationships between flow, luminal volume, and reabsorption which hold at constant blood pressure in single microperfused loops.

As is the case for group 1, so also is the case for groups 2 and 3 experiments; there is no support for causal chain-linking arterial pressure, luminal volume, and reabsorption.

According to the data in Table 4, it seems that norepinephrine infusions in group 2 partially reproduced the effects of chronic hypertension. Luminal volume tended to decrease when arterial pressure and load to the loop increased. The analysis summarized in Table 5, however, does not bear this out. A negative correlation between pressure and volume was looked for but a statistically insignificant positive correlation appeared. Again, there is no evidence that luminal volume correlates directly with reabsorption.

The results of group 3 experiments suggest that hypotension combined with norepinephrine infusion might set up conditions under which luminal volume 0.6 nl greater and a reabsorption rate 2.3 nl/min greater than that for control rats. Blood pressure in the rats with arteriovenous fistulae was 25 mm Hg lower than it was in control rats. It is probable that luminal volume varies with interstitial pressure in these animals. An increase in luminal volume prolongs transit time and increases surface area for water extraction in the descending thin limb. This conclusion is supported by a computer simulation of Henle’s loop (Baines et al, submitted for publication).

For these reasons, it appeared likely that acute changes in arterial pressure would produce positive correlations between luminal volume and reabsorption in Henle’s loop. The effects, however, of acute changes in blood pressure produced by aortic constriction or norepinephrine infusion do not support the hypothesis. Correlations may not have been detected because the changes in luminal volume were small, although in group 1 this is not likely to be the case since the observed changes were opposite in direction to those predicted. It may be due to imprecision of the method used to estimate luminal volume, although the concurrence of estimates using transit time or pressure drop in group 1 supports the qualitative if not the quantitative reliability of the estimates.

It is most likely that major adjustments in interstitial pressure must occur before detectable changes in loop volume occur. These readjustments do not occur during an acute change in pressure of 20 to 30 mm Hg. Perhaps, more than a simple change in perfusion pressure is required. The results obtained in group 3 support this conclusion. So do the observations of Levy [6], who found that with combined renal vasodilation and norepinephrine-induced hypertension there was a decrease in reabsorption and apparent luminal volume in dogs with thoracic vena caval constriction.

Acknowledgments

This work was supported by the Medical Research Council of Canada grant, MA 3045.

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