

Fluid Reabsorption in Henle's Loop and Urinary Excretion of Sodium and Water in Normal Rats and Rats with Chronic Hypertension

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ABSTRACT The function of the short loops of Henle was investigated by micropuncture technique in normal rats, in rats with spontaneous hypertension, and in the untouched kidney of rats with experimental renal hypertension. All animals received a standard infusion of 1.2 ml of isotonic saline per hr.

With increasing arterial blood pressure (range from 90 to 220 mm Hg), a continuous decrease in transit time of Lissamine green through Henle's loop from 32 to 10 sec was observed. Fractional water reabsorption along the loop declined progressively from 26 to 10%, and fractional sodium reabsorption decreased from 40 to 36% of the filtered load. The fluid volume in Henle's loop calculated from transit time and mean flow rate also decreased with increasing blood pressure. There was no change in superficial single nephron filtration rate but there was a slight increase in total glomerular filtration rate (GFR). Sodium and water reabsorption in the proximal tubule remained unchanged.

Urine flow rate, sodium excretion, osmolar clearance, and negative free water clearance increased with increasing blood pressure. The osmolal urine to plasma (U/P) ratio declined but did not fall below a value of 1.5. It is concluded that the increase in sodium and water excretion with chronic elevation of arterial blood pressure is caused by a decrease of sodium and water reabsorption along the loop of Henle, presumably as a consequence of increased medullary blood pressure.

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INTRODUCTION

Most hypertensive patients respond to an intravenous saline load with a more rapid excretion of sodium and water than normotensive individuals (1-7). The mechanism of this response is poorly understood. From experiments in dogs it is evident that acute elevation of renal perfusion pressure causes diminished tubular reabsorption of sodium and water (8). Tobian, Coffee, Ferreira, and Meuli (9) have speculated on the possibility of a hormonal mechanism accounting for the natriuresis, activated by increased perfusion pressure. Other authors (Thurau and Deetjen [10], and Selkurt, Womack, and Dailey [11]) have shown that this type of diuresis is characterized by a decreased negative free water clearance ($T^{\circ}_{H_2O}$). They attributed the "pressure diuresis" to a washout of the medullary osmotic gradient needed for the process of urinary concentration, presumably as a consequence of a higher medullary blood flow. These findings and their interpretation cannot be transferred without risk to the conditions of chronic hypertension. In a previous investigation (12, 13) in rats with Goldblatt hypertension we found that the unclamped kidney exposed to a blood pressure of about 180 mm Hg showed an increased urinary excretion of sodium and water which was similar to that induced by acute elevation of renal perfusion pressure. However, $T^{\circ}_{H_2O}$ also increased. In these animals the high urine volume was due to a marked inhibition of fluid reabsorption along the loop of Henle, which was only partly compensated by a higher than normal fluid reabsorption in the distal tubule and in the collecting duct. In the present study we have investigated more intensively the effect of arterial blood pressure on urinary excretion and on function of Henle's loop over a pressure range from 90 to 220 mm Hg. With Henle's loop we mean that part of

the superficial nephron, which lies between the late proximal and early distal puncture sites.

The following three groups of animals were used: (a) normal rats, (b) rats with a moderate spontaneous hypertension, and (c) rats with experimental hypertension 4–5 wk after clamping one renal artery with a Goldblatt clamp. In the last group, only the untouched kidney, which is exposed to the high blood pressure, was investigated. All animals received an isotonic saline infusion of 1.2 ml/hr. Micropuncture experiments were done on superficial nephrons. Accordingly, only the function of short loops of Henle was studied.

METHODS

The experiments were performed on Albino rats of about the same weight (190–210 g). The animals were divided into three groups differing from each other by the level of arterial blood pressure. For the first group male rats of the FW₄₉ strain (Paderborn) were chosen, having a mean arterial blood pressure between 90 and 110 mm Hg. The second group consisted of female rats of the Wistar strain with a blood pressure from 110 to 160 mm Hg. In the third group female Wistar rats with experimental renal hypertension of 4–5 wk duration (for the method see reference 12, 13) were used, their blood pressure ranging from 160 to 220 mm Hg. In this last group only the untouched kidney

exposed to the high arterial blood pressure was investigated. All animals were kept on the same standard rat diet (Altromin, sodium content: 1200 mg/kg) and had free access to water. The animals were anaesthetized by intraperitoneal injection of Inactin (Promonta-Werk, Hamburg, 70–80 mg/kg body weight) and prepared for micropuncture as previously described (12–14). During surgery the rats received 0.5–1 ml of isotonic saline through a cannula in the jugular vein to compensate for extracellular fluid losses at the surgical sites. The ureter was cannulated with polyethylene tubing (PE 10, Clay-Adams Co., Parsippany, N. J.) and the urine collected in glass vials closed with parafilm "M." The urinary volume was determined by weighing. Blood pressure was measured continuously via a heparin-filled PE 50 catheter in the left common carotid artery, connected to a Statham strain gauge (Statham Instruments, Inc., Oxnard, Calif.). For determination of the glomerular filtration rate (GFR) and the concentration of inulin in tubular fluid, a priming dose of about 30 μ Ci of C¹⁴-labeled inulin carboxylic acid (New England Nuclear Corporation, Boston, Mass.) and a sustaining infusion of 1 μ Ci/min in isotonic saline were administered. The sustaining infusion was delivered at a rate of 0.02 ml/min with a calibrated constant infusion pump (Braun-Apparatebau, Melsungen). For the determination of single nephron GFR the end of the proximal convoluted was punctured using short tipped sampling pipettes and tubular fluid was collected continuously over a period of 3–6 min. All collections (ranging in size from 30 to 70 $\times 10^{-6}$ ml) were made on tubules blocked by the injection of a small, easily movable

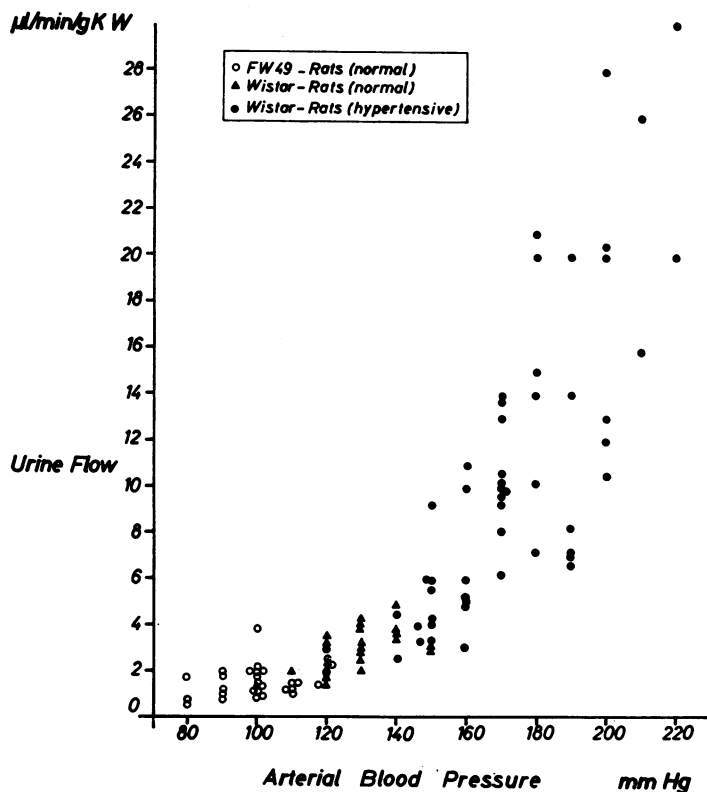


FIGURE 1 Relationship between arterial blood pressure and urine flow rate. KW stands for kidney weight.

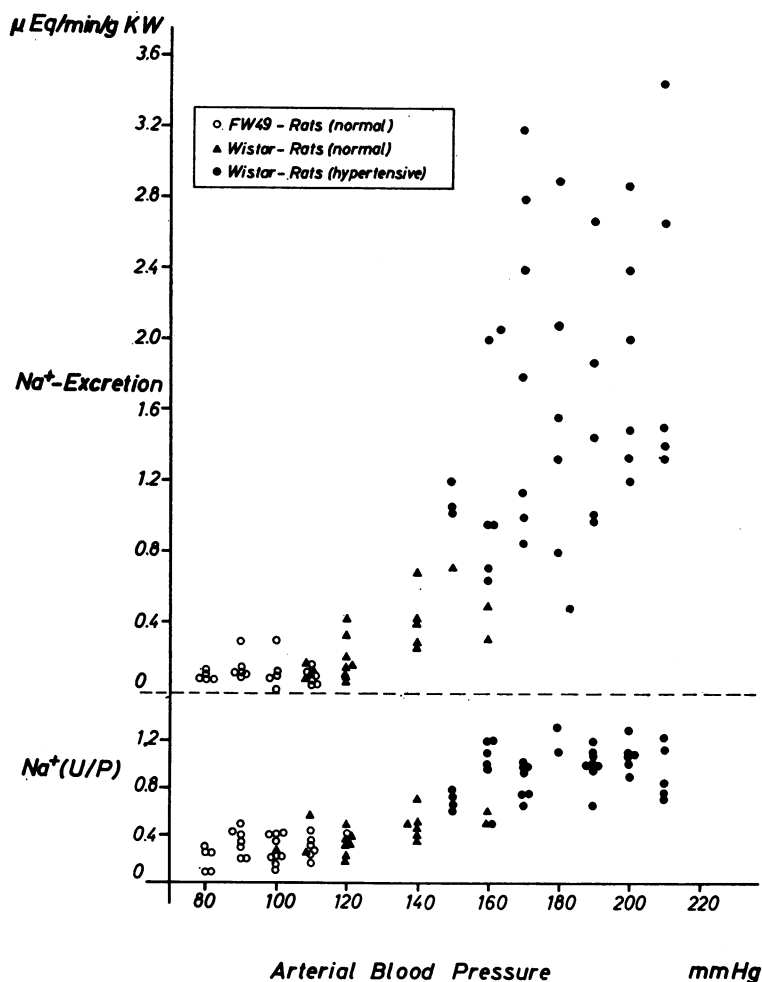


FIGURE 2 Relationship between arterial blood pressure and urinary excretion of sodium (upper part) and U/P Na^+ (lower part).

column of mineral oil into the tubular lumen. Rate of fluid collection was adjusted in such a way as to secure a constant position of the blocking oil droplet.

After collection, the tip of the pipette was sealed with mineral oil from the kidney surface and samples were transferred into a thin-walled constant-bore capillary of 0.2 mm i.d. with the aid of a micromanipulator. The volume of the fluid sample collected was calculated from the length of the fluid column, as measured by an eyepiece micrometer, and the known diameter of the capillary. All microsamples of this series were measured in the same capillary. The end of the proximal convolution was located by observing the passage of Lissamine green through the proximal tubule as described by Gertz, Mangos, Braun, and Pagel (15). With this technique all tubular punctures have been found to be located between 55 and 65% of the total length of the proximal tubule (16).

Single nephron GFR was calculated from the tubule fluid to plasma inulin ratio $(\text{TF}/\text{P})_{\text{In}}$ and volume of tubule fluid (\dot{Q}) collected per minute either from late proximal or early distal

puncture sites using the equation:

$$\text{single nephron GFR} = (\text{TF}/\text{P})_{\text{In}} \times \dot{Q} \quad (1)$$

where single nephron GFR and \dot{Q} are in units of 10^{-6} ml/min.

After collection of distal tubular fluid, the tubule was filled with neoprene (17). Dissection, identification of puncture site, and measurements of tubular length were done according to the procedures described by Gottschalk and Mylle (18). For the calculation of reabsorption in Henle's loop, only samples with a puncture site between 20 to 30% distal tubular length were used. In all animals tubular transit time was repeatedly measured after injection of 0.05 ml of 5% Lissamine green (19). Proximal transit time was measured as previously described (14). The time interval between coloration of the last proximal convolutions and the entrance of the color wave into the first three to five distal tubules was taken as a measure of transit time through Henle's loop. Only in these early visible distal tubules sampling of fluid was performed. Hydrostatic pressure in superficial proximal and distal convolutions was measured using the Landis method (20).

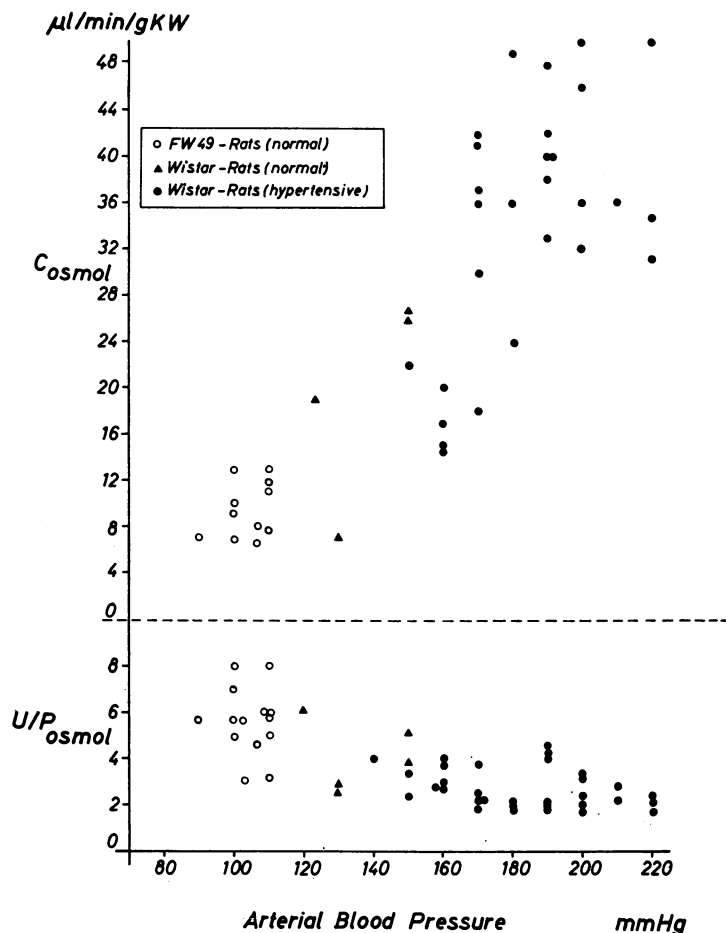


FIGURE 3 Relationship between arterial blood pressure and osmolar clearance (C_{om}) (upper part), and U/P osmol (lower part).

To estimate the size of the proximal and distal tubules the surface of the kidney was photographed while Lissamine green was passing through the tubules. The photographic equipment has been described in a previous paper (14).

In order to measure the activity of inulin- ^{14}C , samples of tubular fluid and plasma were taken up into self-filling micropipettes and transferred into counting vials containing 1 ml of water. 5 ml of a scintillation fluid, composed of two parts of toluene (with 0.4% 2,5-diphenyloxazole [PPO] and 0.005% *p*-bis[2-(5-phenyloxazolyl)]benzene [POPOP]) and one part of Triton-X-100, was added to the water. Radioassay of the samples was done in two channels of a liquid scintillation counter ("Mark I," Nuclear-Chicago Corp., Des Plaines, Ill.) to a total of at least 4000 counts. Mean efficiency for C^{14} was 73%; all samples had an activity of at least twice the background.

Sodium concentration in distal tubular fluid was measured with a dual channel microflame photometer by P. Müller (Wissenschaftlicher Gerätebau, W. Hampel, Berlin). For the measurement of sodium concentration in plasma and urine a standard flame photometer was used (Fa. Eppendorf Gerätebau, Hamburg). Osmolality of plasma and urine was determined in a standard osmometer (Fa. Knauer, Wissen-

schaftlicher Gerätebau, Berlin). Inulin and plasma electrolyte values were corrected for a plasma water content of 94%. A Donnan correction of 0.95 was applied for sodium concentration. The mean values are given with their standard errors (SE).

RESULTS

Urinary excretion, osmolar clearance, and $T^{\text{H}_2\text{O}}$. Urine flow rate, sodium excretion, and osmolar clearance in relation to blood pressure are shown in Figs. 1-3. All three parameters were markedly elevated at high blood pressure. Urine osmolality, as demonstrated in the lower part of Fig. 3, declined at higher blood pressure. However, U/P osmol never fell below a value of 1.5.

The relationship between the negative free water clearance ($T^{\text{H}_2\text{O}}$) and arterial blood pressure is shown in Fig. 4. It is evident that $T^{\text{H}_2\text{O}}$ increases, i.e., more water is lost from the collecting ducts at higher blood

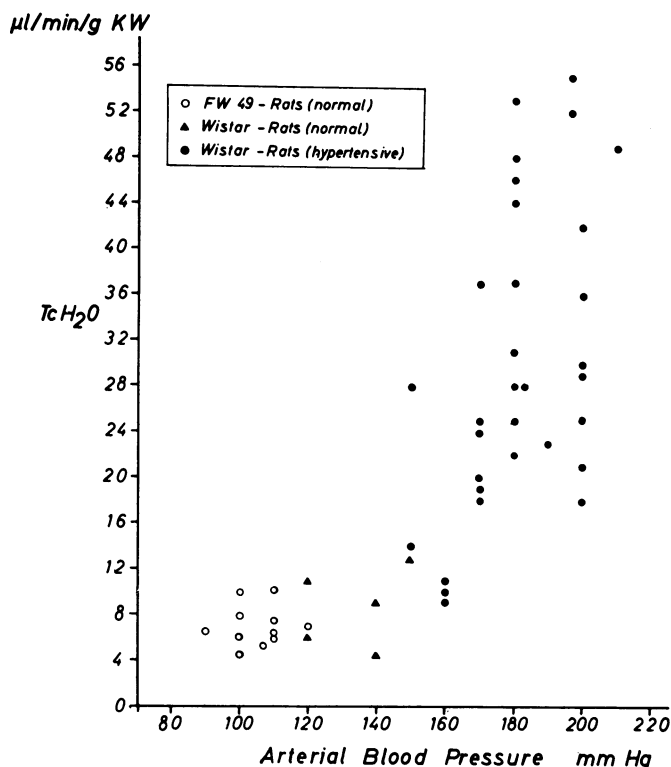


FIGURE 4 Relationship between arterial blood pressure and "negative free water clearance" (T_{cH_2O}).

pressure level. This finding is in contrast to data obtained during acute elevation of renal perfusion pressure showing a progressive decrease of T_{cH_2O} as pressure is elevated (10, 11).

The data graphed in Figs. 1-4 represent the mean values of the second and third period of urine collection (see Fig. 5). In those experiments in which only the second collection period could be completed, these data were also included in the figures. In Fig. 5, the time course of urine flow rate and sodium excretion during the experiments is demonstrated. In all three groups of animals, differing in their blood pressure levels, a continuous rise in urine flow rate and sodium excretion was observed. However, the increment was steepest in the group with the highest blood pressure and the sodium and water excretion of this group was always much higher than in the normotensive group, even in the first collection period, i.e., 50 min after the start of the infusion.

Transit time through Henle's loop and fractional sodium and water reabsorption. Fig. 6 demonstrates the effect of arterial blood pressure on transit time through Henle's loop and through the proximal convolution. With increasing blood pressure transit time

through the loop decreased from a normal value of about 32 sec to an average value of 10 sec at a blood pressure of 220 mm Hg. Proximal transit time remained unchanged (11.5 ± 0.23 sec) as indicated in the lower part of Fig. 6. Parallel to these changes there was a progressive decline in fractional water and sodium reabsorption along Henle's loop. In Fig. 7 late proximal (lower part) and early distal (upper part) TF/P-inulin ratios are plotted on the left ordinate and fractional water reabsorption on the right ordinate. As shown in the lower part of Fig. 7, late proximal TF/P-inulin ratios remained unchanged over the observed pressure range (2.18 ± 0.05), i.e., fractional reabsorption of sodium and water in this part of the nephron was not influenced by an increase in arterial blood pressure. However, as can be seen from the upper part of Fig. 7, early distal TF/P-inulin ratios declined with increasing arterial blood pressure. At a blood pressure of 100 mm Hg an early distal TF/P-inulin ratio of 5.1 is obtained from the regression line, a value which is in good agreement with the results of other authors (21, 22). At a blood pressure of 200 mm Hg, TF/P-inulin was only 2.9 meaning that fractional water reabsorption of the loop of Henle had decreased from 26 to 11.5% of the

filtered load. Fractional water reabsorption of Henle's loop was calculated from the expression:

$$\text{per cent H}_2\text{O reabsorption} = \left[\frac{(1 - P/TF_{\text{In distal}})}{(1 - P/TF_{\text{In proximal}})} \right] \times 100 \quad (2)$$

Fractional reabsorption of sodium along the loop (upper part of Fig. 8) decreased from 40 to 36% of the filtered load. There was no relationship between the level of arterial blood pressure and early distal sodium concentration. As is demonstrated in the lower part of Fig. 8, early distal Na^+ TF P ratio averaged 0.36 ± 0.028 at a normal pressure range and 0.3 ± 0.022 at the highest blood pressure. However this difference was not statistically significant.

Single nephron GFR and total GFR. In order to exclude the possibility that the shortened transit time through the loop of Henle associated with increasing

blood pressure was the result of an augmented flow rate into the loop, filtration rates of superficial single nephrons were estimated. The data are summarized in Fig. 9 (upper part). No change in single nephron GFR could be observed over the range of blood pressure investigated. The mean value of $30.5 \pm 2.04 \times 10^{-6}$ ml/min per g kidney weight (KW) is lower than that reported by Flanigan and Oken (23), Glabman, Aymedjian, and Bank (24), and Oken, Arce, and Wilson (25), and is slightly higher than that found by Horster and Thureau (26). This disagreement may be due to the different salt content of the rat diet, fed in the various laboratories (26). In the lower part of Fig. 9 total GFR is plotted as a function of blood pressure. With increasing blood pressure there was a slight increase in total GFR from a normal mean value of 1.06×10^{-6} ml/min per g KW to a mean of 1.17×10^{-6} ml/min per g KW at the highest blood pressure ($P < 0.01$).

Proximal and distal tubular diameter and hydrostatic pressure. Proximal intratubular pressure remained constant (14 ± 0.18 mm Hg) over the observed range of arterial blood pressure (Fig. 10). There was no difference between the results, whether the renal capsule was removed or left intact. Distal intratubular pressure rose slightly from a mean of 5.5 ± 0.11 mm Hg at a blood pressure level between 100 and 140 mm Hg, to a mean of 6.7 ± 0.2 mm Hg at a pressure level between 150 and 200 mm Hg ($P < 0.01$). Proximal tubular diameter under free flow conditions as shown in the lower part of Fig. 11 was found to be unchanged ($19 \pm 0.29 \mu$). However, distal tubules (upper part of Fig. 11) were slightly wider at a high pressure level ($17 \pm 0.3 \mu$) than under normal conditions ($14.5 \pm 0.33 \mu$) ($P < 0.01$).

DISCUSSION

All of the rats used in the present experiments received the same amount of saline but the urinary excretion rates of sodium and water differed grossly in the different groups of rats. A very obvious correlation existed between the arterial blood pressure and the urinary excretion of solutes and water.

The increased urine flow rate and excretion of solutes, particularly sodium, of the hypertensive group could not be accounted for by changes of either single nephron or total filtration rate or of proximal tubular reabsorption. In this respect our findings are comparable with results obtained during acute elevation of arterial blood pressure in the dog (27) but not in the rat. In the rat, acute elevation of arterial blood pressure has been reported to result in an inhibition of proximal reabsorption (28).

If the flow rate at the end of the proximal convolution is independent of blood pressure, then the increased

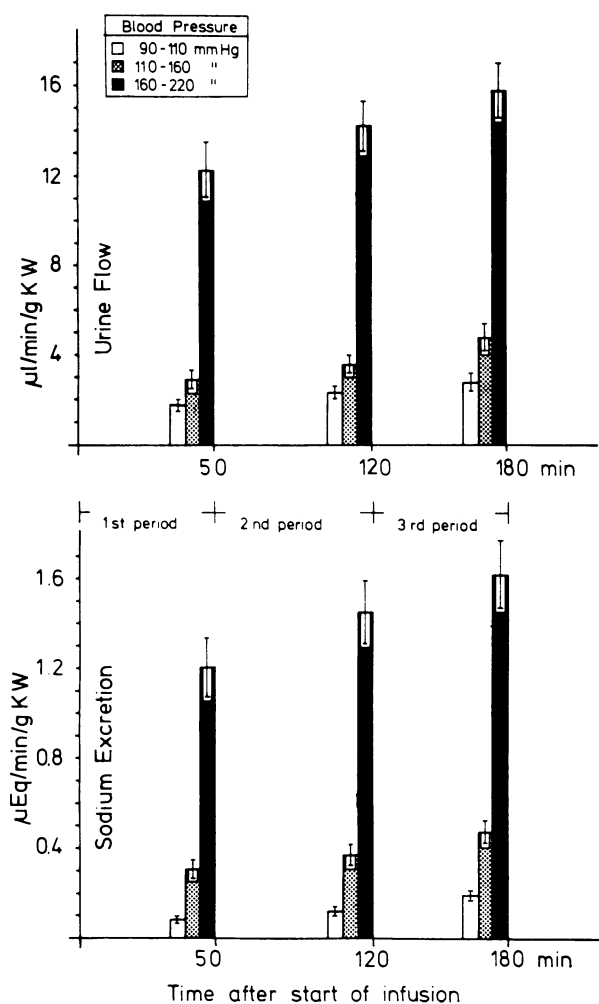


FIGURE 5 Urine flow rate and sodium excretion in the different groups of rats during the time of the experiments.

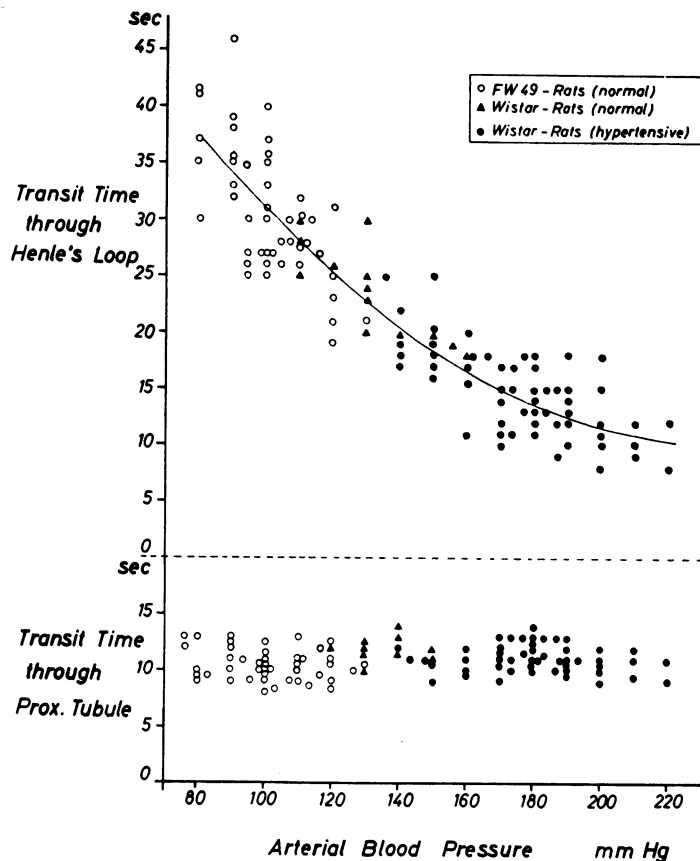


FIGURE 6 Relationship between arterial blood pressure and transit time through the proximal convolution (lower part) and through the loop of Henle (upper part). The regression line for the transit time through Henle's loop is described by $y = 72.31 - 0.524x + 0.0011x^2$.

urinary excretion observed in the chronically hypertensive rats must be due to a diminished reabsorption somewhere in the more distal parts of the nephron. According to our experiments, the site of this change is the loop of Henle. Early distal TF/P-inulin ratios decreased significantly with increasing blood pressure (Fig. 7).

In this series of experiments, tubular fluid from only the first 20–30% of distal tubular length was analyzed. Accordingly, a relatively small number of values was obtained. It is possible, however, to estimate the TF/P-inulin ratio at the beginning of the distal tubule by extrapolating the regression line of TF/P-inulin ratios along the whole length of the distal tubule. This has been done in an earlier set of experiments demonstrating a similar diminution of early distal TF/P-inulin ratios in the unclipped kidney of chronically hypertensive rats (12, 13).

Since the early distal sodium TF/P ratio was unaltered (Fig. 8, lower part), fractional sodium reab-

sorption along the loop was also reduced at high arterial pressure (Fig. 8, upper part). However, while fractional water reabsorption declined from about 26 to 12% as blood pressure was elevated from 100 to 200 mm Hg, fractional sodium reabsorption decreased only from about 40 to 36%. This is probably due to the different behavior of the two limbs of the loop. If, in the descending limb, a rise in blood pressure diminishes net water and sodium reabsorption to the same extent, more water and sodium would be delivered to the ascending limb. From the study of Morgan and Berliner (29), it can be inferred that the net reabsorption of sodium in the ascending limb increases at a higher load. If this is accepted and if the ascending limb is actually water impermeable, the difference in fractional reabsorption of water, respectively sodium, would readily be explained.

The data from the clearance measurements are in accordance with the results obtained by micropuncture. C_{osm} , which was markedly elevated at high arterial pressure (Fig. 3), measures the minimum volume of

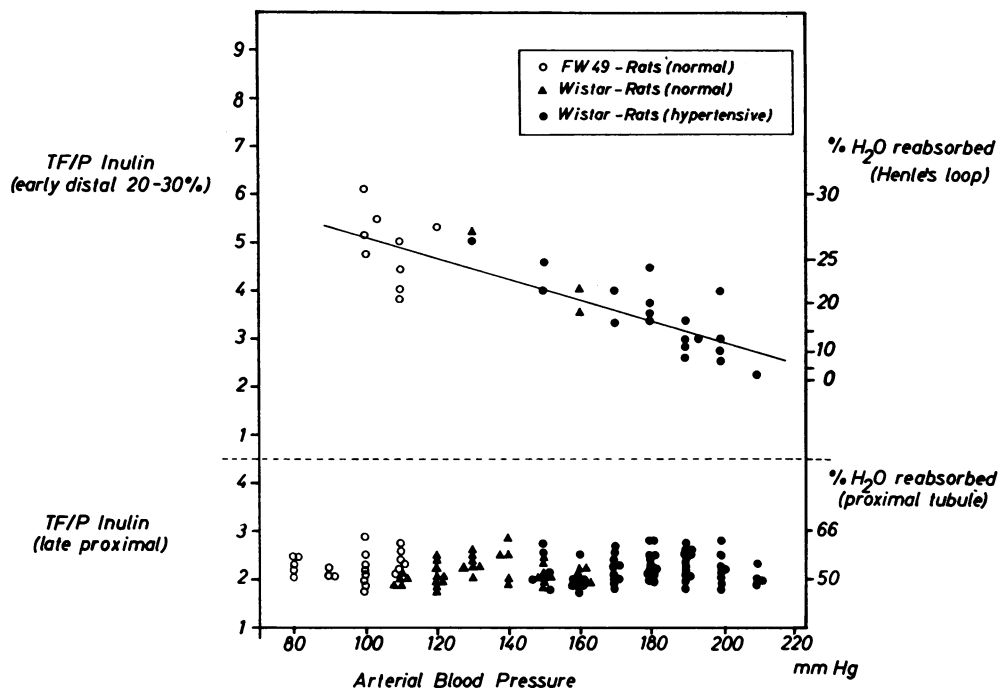


FIGURE 7 Relationship between arterial blood pressure and fractional water reabsorption in the proximal convolution (lower part) and along the loop of Henle (upper part). The regression line for the upper part is described by $y = 7.38 - 0.0219x$. The slope of this line is significantly different from zero ($P < 0.01$).

fluid issuing from the distal convoluted tubule and entering the collecting ducts. At high arterial pressure, the TF/P-inulin ratio was reduced to half its normal value, not only at the beginning but also at the end of the distal tubule (12, 13), indicating that about twice the normal amount of fluid is reabsorbed there and also about twice as much fluid enters the collecting duct. $T^{\circ}H_2O$, which represents the least volume of water transported from the collecting ducts into the medulla, increased with increasing blood pressure (Fig. 4). This again agrees with the results of the earlier investigation (12, 13) but is in contrast to the findings in acute hypertension. During acute elevation of renal perfusion pressure, $T^{\circ}H_2O$ decreases (10, 11). This decrease has been thought to be responsible for the augmented urine flow rate (10). In this connection it should be mentioned that C_{osm} and $T^{\circ}H_2O$ are calculated from the urinary excretion of all nephrons while the micropuncture data in this and in the earlier paper (12, 13) are relevant to the function of superficial nephrons only. In a recent study (30) we found under the same experimental conditions that, at a blood pressure of 180 mm Hg, glomerular filtration rate of the juxtamedullary nephrons was more than twice that at normal pressure. An increased juxtamedullary GFR could not only explain the slight increase in total GFR (Fig. 9, lower part) but could

also contribute to the observed increase of C_{osm} and $T^{\circ}H_2O$.

We believe that the results presented in this paper point to a more or less direct inhibitory effect of chronic hypertension on the reabsorption along the short loops of Henle. But since most of the data were obtained from the unclamped kidney of rats with Goldblatt hypertension, it is open to question whether the results apply to other types of chronic hypertension as well. Nevertheless, it is noteworthy that the few data which could be obtained from rats with spontaneous hypertension fit into the general pattern (see the black triangles in the figures).

We have no direct evidence as to how chronic hypertension affects the reabsorption in the loop. An intermediary, humoral factor cannot be completely ruled out. However, since in the clamped kidney of hypertensive rats the reabsorption of sodium and water along the loop is quite normal (12), a humoral factor of extrarenal origin is most unlikely. This view agrees with that of Cottier, Weller, and Hoobler (6). From studies on patients with essential hypertension, these authors thought it more likely that a rise in pressure within the renal vessels acts directly to augment the tubular rejection of sodium chloride and water.

Since cortical blood flow seems to be well auto-

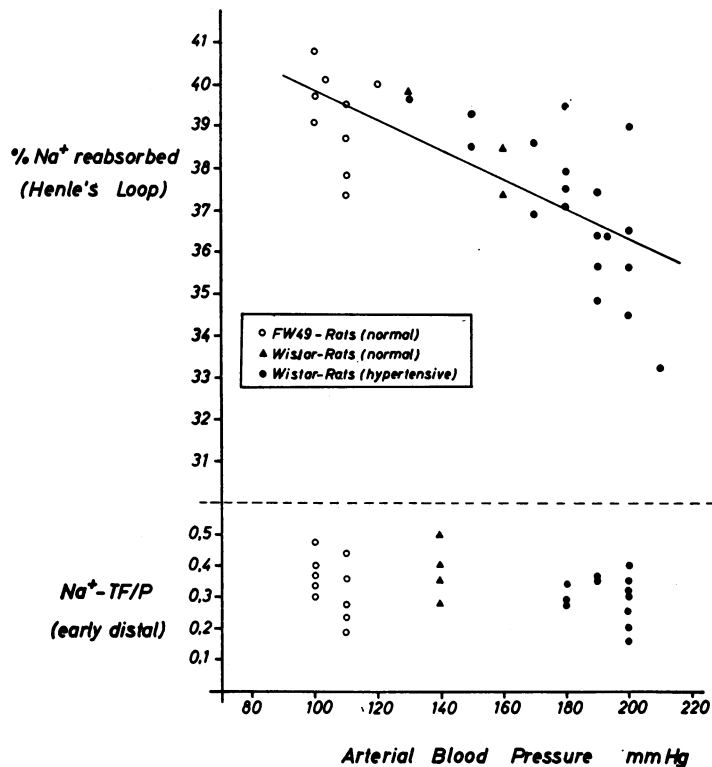


FIGURE 8 Relationship between arterial blood pressure and fractional Na^+ -reabsorption in the loop of Henle (upper part). The regression line is described by $y = 43.45 - 0.035x$. The slope of this line is significantly different from zero ($P < 0.01$). In the lower part early distal $\text{Na}^+ - \text{TF}/\text{P}$ is plotted on the ordinate.

regulated, it is reasonable to assume that circulatory changes within the kidney during chronic hypertension will affect mainly the medullary circulation. According to the experiments of Thureau, Deetjen, and Kramer (31), blood flow through the renal medulla does not exhibit autonomy and increases when renal perfusion pressure is raised acutely. Similar results have been obtained in chronically hypertensive rats. In a parallel series of experiments in our laboratory it has been demonstrated that not only juxtamedullary GFR (30) but also blood flow into the medulla (outer and inner zone) is augmented considerably while no change in cortical blood flow could be observed (32). It is quite conceivable that these changes in the medullary circulation are responsible for the diminished reabsorption along the short loops of Henle.

One explanation of the reduced fluid reabsorption along Henle's loop in chronic hypertension may involve a medullary washout of sodium and other solutes. If medullary blood flow increases at higher blood pressure and there is a washout of solutes, medullary hypertonicity should decrease and the amount of water leaving the

descending limb should decline. However, most of the loops from the superficial nephrons reach only into the outer zone of the medulla. The maximum osmotic concentration here is probably not more than twice that of plasma. Accordingly, changes in osmotic concentration in this region can only be relatively small and will probably not alter, to a large degree, the fluid reabsorption from the loops. In the unclipped kidney of chronically hypertensive rats only a small, statistically not significant decrease in tissue osmolality was observed in the outer medulla (32). Furthermore, even in rats with diabetes insipidus having no appreciable medullary osmotic gradient, fractional water reabsorption along the short loops averaged 24% (33), a figure quite comparable with those obtained from nondiuretic, normotensive rats. It seems doubtful therefore that the marked inhibition of fluid reabsorption from Henle's loop in chronic hypertension is due to a washout of osmotically active substances in the medulla. On the other hand, a washout did exist at high blood pressure, at least in the papilla. Final urine is thought to be in osmotic equilibrium with papillary tissue. Urine osmolality was significantly lower

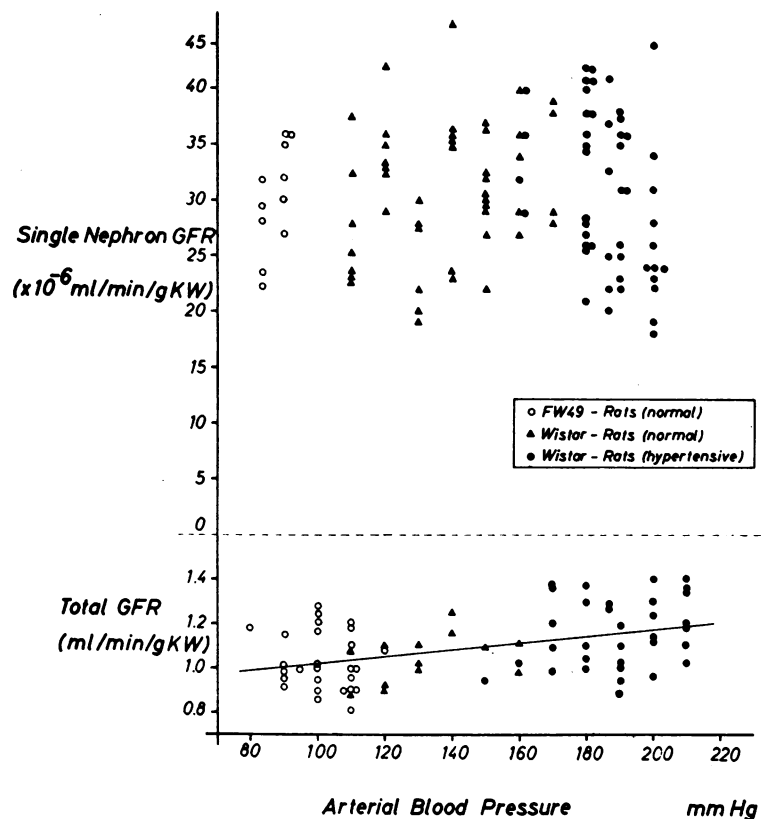


FIGURE 9 Relationship between arterial blood pressure and single nephron GFR (upper part) and total GFR (lower part). The regression line for total GFR is described by $y = 0.866 + 0.0015 x$.

at high than at normal blood pressure (Fig. 3). Similar changes were observed in papillary tissue osmolality (32).

Another explanation may involve an increased medullary blood and/or interstitial pressure. In the absence of medullary autoregulation pressure will rise in those capillaries which originate from the juxtamedullary glomeruli and surround the short loops of Henle. As proposed by Earley et al. (34, 35) and Lewy and Windhager (36), such a change in the hydrostatic pressure gradient could result in a reduction of sodium and water reabsorption. Furthermore, as already mentioned, juxtamedullary filtration rate is strikingly elevated in chronic hypertension (30). Therefore, the volume of the juxtamedullary proximal tubules can be expected to be enlarged at high blood pressure. According to the data of Moffat and Fourman (37), these convolutions are lying within the inner zone of the cortex and the outer stripe of the medulla, i.e., in the same region where both the thick ascending and descending limbs are found. Thus, an increment of juxtamedullary tubular volume may also lead to an increase in the interstitial pressure. In this connection it should be mentioned that very small hydro-

static pressure gradients affect the rate of active sodium transport across the frog skin (38).

There is one observation in our experiments which points indirectly to an increased peritubular pressure around the short loops in chronic hypertension. This is

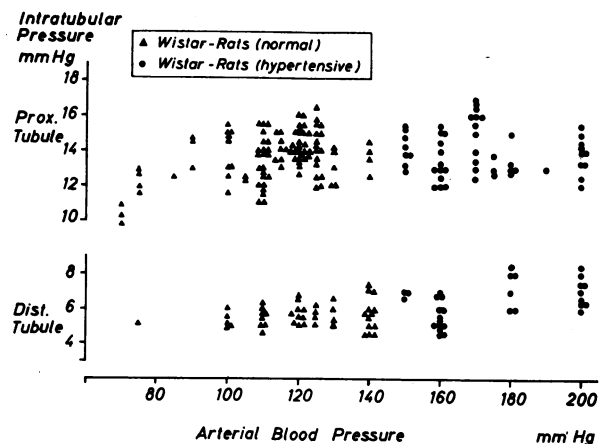


FIGURE 10 Relationship between arterial blood pressure and proximal and distal intratubular pressure.

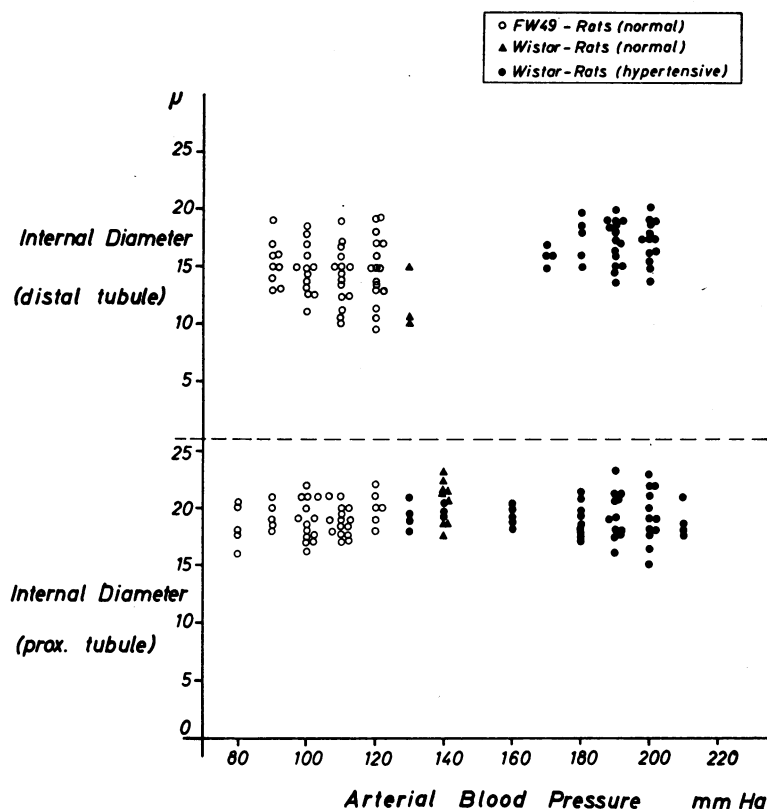


FIGURE 11 Relationship between proximal (lower part) and distal (upper part) tubular diameter under free flow conditions.

the reduced transit time through the loops. Since single nephron GFR and fractional water reabsorption in the proximal tubule were unaltered at elevated blood pressure, the flow rate at the beginning of Henle's loop was also unaltered. However, the transit time through the loop declined from 32 to 12 sec as blood pressure was elevated from 100 to 200 mm Hg (Fig. 6). This finding is difficult to explain without assuming that the volume of Henle's loop decreased.

If the transit time of Lissamine green, measured in the usual manner, can be taken as the mean transit time, the volume of the loop can be estimated from the following equation:

$$V = T(\dot{Q}_{\text{prox}} - \dot{Q}_{\text{dist}}) / \ln(\dot{Q}_{\text{prox}} / \dot{Q}_{\text{dist}}) \quad (3)$$

In this equation, V is the volume of Henle's loop; T , the mean transit time; \dot{Q}_{prox} , the flow rate at the end of the proximal convolution; and \dot{Q}_{dist} , the flow rate at the beginning of the distal convolution. Substituting values derived from our experiments, one obtains a volume of 3.5×10^{-6} ml at 100 mm Hg and 1.7×10^{-6} at an arterial pressure of 200 mm Hg. It is doubtful, how-

ever, whether the use of this equation is justified.¹ In equation 3 the assumption is made that the distribution of the reabsorptive process along the loop is uniform. This is probably a gross oversimplification. Nevertheless, the observed decrease in transit time cannot be explained solely by an increased mean flow rate due to a reduced net reabsorption of water. If the volume of Henle's loop remained constant, the transit time could decrease only to 22 sec even in the extreme case where no water at all is reabsorbed in the loop, i.e., $\dot{Q}_{\text{dist}} = \dot{Q}_{\text{prox}}$. We therefore conclude that the marked reduction in loop transit time observed at high blood pressure signifies a diminution in the volume of the loop. It remains open to question whether this decrease in volume, according to the geometry hypothesis of Gertz (39), leads in itself to the observed reduction in fluid reabsorption.

In this connection it is interesting to note that the resistance to flow in what we call Henle's loop did not increase although the volume apparently declined with increasing arterial pressure. The hydrostatic pressure gradient along the loop (proximal minus distal intra-

¹ For this reason, no details of the calculation are given.

tubular pressure) did not change until an arterial pressure of 160 mm Hg was reached, above which it actually decreased due to a slight rise in distal intratubular pressure (Fig. 10). Thus, resistance to flow was lower at high blood pressure than at normal blood pressure although apparently the radius was smaller. No explanation for this discrepancy can be offered. However, Henle's loop probably cannot be considered to be a uniform tube. Resistance to flow may reside only in a very small part (40) and volume changes may be unevenly distributed. The slight increase in distal intratubular pressure (Fig. 10) and in the diameter of the distal tubule (Fig. 11) above an arterial pressure of 160 mm Hg is thought to be the consequence of the high urine flow. This mechanism was originally proposed by Gottschalk and Mylle (40).

Our considerations may be summarized as follows: chronic hypertension, without vascular damages in the kidney, leads to an elevated medullary blood pressure. As a consequence, sodium and water reabsorption along the short loops of Henle decreases and juxtamedullary glomerular filtration increases. Both changes will augment the load to the distal tubule. This increased load may be more or less completely compensated by a higher reabsorption along the distal tubule and the collecting ducts but will lead to a tendency of the kidney to excrete more water and sodium. Under basal conditions, urinary excretion may be only slightly elevated depending on the uptake of salt and water; under a larger load, however, the hypertensive kidney will excrete sodium and water more promptly than a normotensive one.

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