Functional Correlates of Compensatory Renal Hypertrophy

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ABSTRACT The functional correlates of compensatory renal hypertrophy were studied by micropuncture techniques in rats after the removal of one kidney. The glomerular filtration rate increased to roughly the same extent in the whole kidney and in individual surface nephrons, resulting in a greater amount of sodium delivered to the tubules for reabsorption. The fraction of the glomerular filtrate absorbed [determined from the tubular fluid–to–plasma ratio (TF/P) for inulin] remained unchanged in both proximal and distal portions of the nephron. The way in which the tubules adjusted to nephrectomy, however, differed in proximal and distal convolutions. After nephrectomy, the reabsorptive half-time, indicated by the rate of shrinkage of a droplet of saline in a tubule blocked with oil, was unchanged in the proximal tubule but significantly shortened in the distal convoluted tubule. Nevertheless, steady-state concentrations of sodium in an isolated raffinose droplet in the distal as well as the proximal tubule were the same in hypertrophied kidneys as in control animals. Possible reasons for this paradox are discussed.

Transit time through the proximal tubules was unchanged by compensatory hypertrophy, but transit time to the distal tubules was prolonged.

Changes in renal structure resulting from compensatory hypertrophy were also found to differ in the proximal and the distal portions of the nephron. Although tubular volume increased in both portions, the volume increase was twice as great in the proximal tubule as in the distal. In order, therefore, for net reabsorption to increase in the distal tubule, where the changes in tubular volume are not so marked, an increase in reabsorptive capacity per unit length of tubule is required. This increase is reflected in the shortening of reabsorptive half-time in the oil-blocked distal tubule that was actually observed.

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INTRODUCTION

When renal tissue is removed or damaged, the nephrons that remain grow in size and change in function. The rate of filtration through their glomeruli increases. After unilateral nephrectomy, for example, glomerular filtration rate in the remaining kidney usually increases by 40–70%; total filtration rate approaches 70–85% of the amount previously filtered by both intact kidneys (1, 2). The kidney enlarges by a process involving both hypertrophy and hyperplasia (3). The increase in glomerular filtration, however, quickly, outstrips the increase in kidney size and weight (2, 4). Most of the additional fluid filtered is reabsorbed, so that the work of reabsorbing sodium and water per gram of viable kidney tissue is greatly increased in compensatory hypertrophy.

The processes involved in the adaptation of renal tubules to this increase in reabsorptive work were studied in the present experiments by the techniques of micropuncture. The mechanisms of adjustment were found to differ in the proximal and the distal convoluted tubules. These differences appear to be related to different changes in tubular anatomy stimulated by renal hypertrophy.

METHODS

Male Sprague Dawley rats weighing 200–400 g were studied by micropuncture techniques. In one group of

rats the right kidney was removed 2–4 wk before micropuncture studies. The weight of the remaining kidney increased by an average of 33% in this time (2). Anesthesia was induced with Inactin (160 mg/kg), a tracheostomy was performed, and the bladder was cannulated with polyethylene tubing. The left kidney was exposed, the capsule stripped, and the kidney immobilized in a plastic cup as previously described (5). During surgery, isotonic saline equal to 1% of the body weight was infused intravenously to compensate for losses of extracellular fluid. A sustaining infusion of isotonic saline at 1.2 ml/hr was continued during the entire experiment.

Glomerular filtration rate (GFR) and tubular fluid–to–plasma ratios (TF/P) of inulin were measured using inulin-methoxy-^{3}H (New England Nuclear Corp., Boston, Mass.). After a priming dose of 75 μc, inulin-^{3}H was infused at a rate of 75 μc/hr. The filtration rate in individual nephrons was measured by collecting samples of proximal tubular fluid during timed intervals that varied from 2 to 4 min. The radioactivity of samples in Bray's solution was determined in a Tri-Carb liquid scintillation spectrometer. Counts were corrected for quenching using a ^{3}H internal standard. Urine was collected at intervals of approximately 30 min, and samples of blood were taken from the tail before and after each collection.

The inulin TF/P ratio was determined in proximal and distal tubules and the urine-to-plasma ratio (U/P) from urine collected via the bladder catheter. Samples of proximal tubular fluid were collected from the last accessible portion of the tubule. This site was identified, after injecting 10% lissamine green, by the convergence of the columns of dye on the kidney surface. The distal tubules were identified as those tubules that filled with concentrated dye after the initial clearing phase. After the sample was obtained the tubule was injected with silicone rubber and catalyst (Canton Bio-Medical Products, Canton, Mass.) and the site of puncture determined by microdissection (6).

The time taken for fluid to pass through the first 55–60% of the proximal tubules (proximal transit time) was measured by the modification of Gertz, Mangos, Braun and Pagel, using 10% lissamine green (7). Distal transit time was measured from the initial glomerular blush to the time when dye first appeared in the distal tubules.

The reabsorption half-time ($t_{\frac{1}{2}}$) of isotonic saline in split-droplet microperfusions of single proximal and distal tubules was measured by sequence photomicrography as described by Gertz (8). The diameter of the oil column adjacent to the isolated droplet was measured in enlarged photographs and expressed in microns by comparison with a stage micrometer photographed at the same magnification. In order to measure the tubular concentration of sodium under steady-state conditions, stopped-flow microperfusion experiments were performed with raffinose in the tubular droplet, as previously described (9). A segment of proximal tubule previously filled with oil was perfused with a solution containing 100 mmoles of raffinose per liter and 100 mEq of NaCl per liter. In the distal tubules a solution containing 200 mmoles of raffinose per liter and 50 mEq of NaCl per liter was used. At least 45 sec was allowed for equilibrium before fluid was collected from the stationary droplet. The distal tubules were identified, as in the inulin studies, by the characteristic appearance of lissamine green after intravenous injection. No attempt was made to localize the portion of tubular epithelium exposed to the perfusing solution, since a variable portion extending beyound the puncture site was exposed.

Sodium concentration in the tubular fluid was measured by ultramicroflame photometry (10). Since the presence of raffinose enhanced the flame emission in samples of proximal tubular fluid, raffinose was added to the standards used in calibration. The presence of an additional interfering substance was found in samples of distal tubular fluid. This impurity was corrected for by using a resampling technique in which the sample was compared to mixtures of the sample plus known standard solutions. Serum values of Na were determined on an internal standard flame photometer and corrected for the serum content of water and the Gibbs-Donnan factor to obtain values for sodium in an ultrafiltrate of serum.

The tubular diameters of the proximal and distal convoluted tubules were measured during free flow by snap-freezing the whole kidney at -70°C and freeze-substituting with absolute alcohol at the same temperature. Histological sections were prepared and were measured with an ocular filar micrometer. Only surface tubules cut transversely were chosen for measurement. Tubular diameters were also measured from color photomicrographs of the kidney surface in vivo after the intravenous injection of 10% lissamine green. The transparencies were projected onto a white screen and the luminal border measured in microns, by comparing it with a stage micrometer photographed at the same magnification.

Tubular length was measured in tubules microdissected from formalin-fixed kidneys using the method described by Oliver, MacDowell, and Tracy (11).

RESULTS

Urine volume and glomerular filtration rate (Table I, Fig. 1.). The rate of urine formation was 4.4 ± 0.5 μl/min per kidney (mean ± SE) in control rats with both kidneys and 7.0 ± 0.8 μl/min in uninephrectomized rats. The urine flow of a single hypertrophied kidney was thus 60% greater than that of one normal control kidney.

The rate of glomerular filtration in the remaining kidney was 92% higher than in the control kidney of intact rats. GFR per kidney in control rats was 358 ± 26.8 μl/min per 100 g of body weight and 689 ± 60.9 μl/min per 100 g of body weight in uninephrectomized animals. The filtration rate determined in individual surface nephrons rose similarly after uninephrectomy, measuring 45.2 ± 3.5 mμl/min in control animals

and 78.8 ± 9.2 mμl/min in rats with one remaining kidney. In order to compare the changes in surface nephrons with those taking place in the whole kidney and to examine the validity of extrapolations from micropuncture findings in surface nephrons, the value for GFR per kidney was divided by the number of nephrons in a rat kidney [27,000 (12)] and compared in 19 instances to the inulin clearance as determined simultaneously by micropuncture of a single surface nephron (Fig. 1). In some cases there were marked discrepancies between the calculated and the measured GFR per nephron, but there was no apparent systematic difference between the two sets of values either before or after nephrectomy.

Transit time (*Table I*). The time taken for fluid to pass through the first 55–60% of the proximal tubule was not significantly different in control rats (8.5 ± 0.4 sec, mean ± SE) from that in uninephrectomized animals with single hypertrophied kidneys (8.8 ± 0.5 sec). The similarity in time of transit through the proximal tubule in the two groups despite an increase in both diameter and length (see below) of the proximal tubule in hypertrophied kidneys suggests that the volume of the proximal tubule increased in proportion to the increase in the rate of glomerular filtration. A similar proportionality was not seen, however, when distal transit time, which includes the rate of flow through the loop of Henle, was measured. The transit time to visible portions of the distal tubule was 51.6 ± 1.6 sec in control rats but was prolonged to 89.2 ± 4.8 sec in uninephrectomized animals ($P < 0.001$).

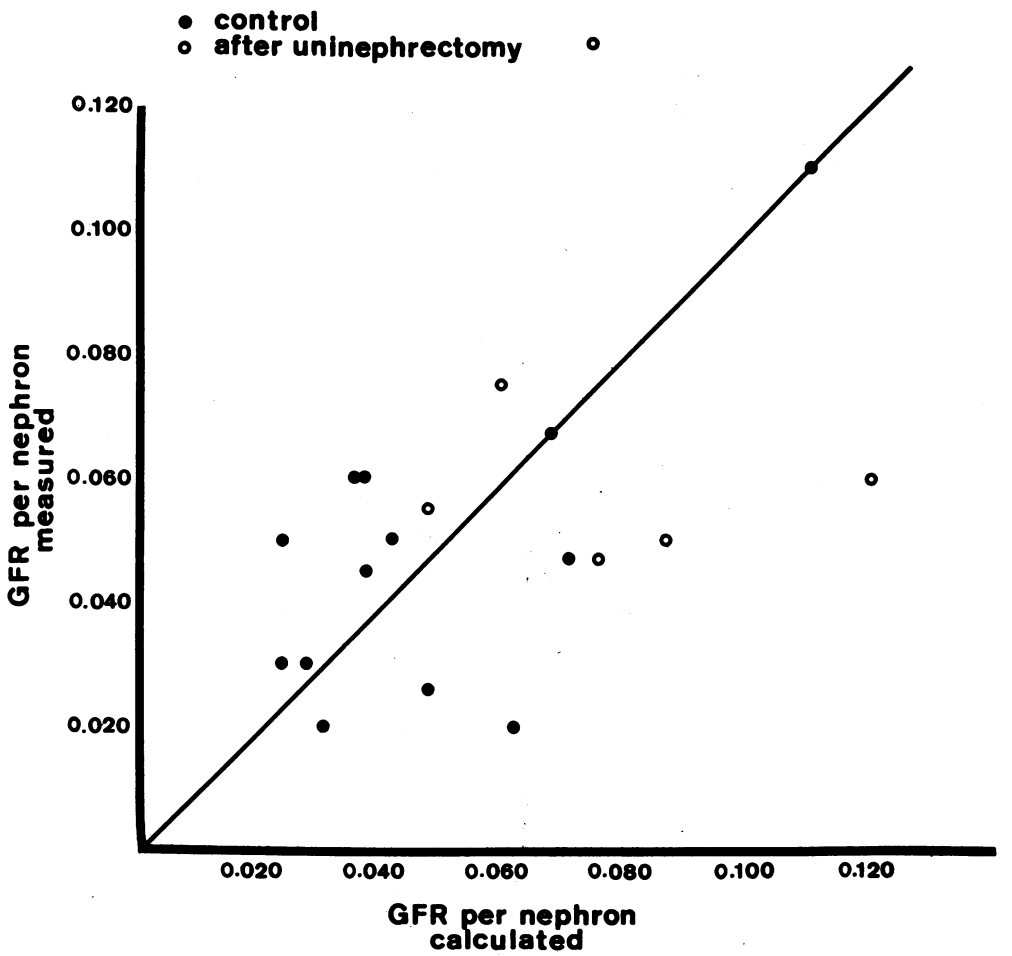

FIGURE 1 Correlation before and after uninephrectomy between inulin clearance (C_{In}) per nephron, calculated from the inulin clearance per kidney, and C_{In} per nephron, measured at the same time in an individual surface nephron by micropuncture. The heavy diagonal line indicates exact correspondence.

TABLE I

Functional Changes during Free Flow

	Urine volume	C_{In} per kidney	C_{In} per nephron	Transit Time: Proximal tubule	Transit Time: Distal tubule
	μl/min per kidney	*μl/min per 100 g body weight*	*mμl/min*	*sec*	*sec*
Control	4.4 ± 0.5 (n = 29)	358 ± 26.8 (n = 25)	45.2 ± 3.5 (n = 27)	8.5 ± 0.4 (n = 21)	51.6 ± 1.6 (n = 25)
Uninephrectomy	7.0 ± 0.8* (n = 29)	689.2 ± 60.9* (n = 18)	78.8 ± 9.2* (n = 17)	8.8 ± 0.5 (n = 12)	89.2 ± 4.8* (n = 13)

Values represent means ± standard error. n, number of observations; C_{In}, inulin clearance.
* Significantly different from control $P < 0.001$.

Tubular dimensions during free flow (Table II). Studies were performed on snap-frozen kidneys to determine the effect of hypertrophy on tubular diameter during free flow. The luminal diameter of the proximal tubule was 25.7 ± 0.5 μ (mean ± SE) in control rats and 30.1 ± 0.8 μ in the experimental group, indicating a 17% ($P < 0.001$) increase associated with hypertrophy. The increase in diameter involved both luminal and outside tubular dimensions and thus differed from the tubular widening observed during saline diuresis, when luminal diameter is increased, but the outside diameter remained the same (13). The changes in the distal convoluted tubule were found to be slightly less than those observed in the proximal tubule. The luminal diameter was 20.2 ± 0.5 μ in the control animals and 22.7 ± 0.6 μ in the uninephrectomized rats ($P < 0.01$). The outside diameter showed a similar change.

The luminal dimensions during free flow were determined by an alternative method, that is, by measuring the tubules on the photographed surface of the kidney in vivo, as a further check on the proportional changes which occur as a result of hypertrophy. By this method the proximal luminal diameter was 14.7 ± 0.4 μ in control kidneys and 16.9 ± 0.3 μ in hypertrophied kidneys, indicating a 15% increase ($P < 0.001$). In the distal tubule, however, no difference was found between the two groups. The diameter of the distal lumen in con-

TABLE II

Dimensional Changes in Proximal and Distal Tubules during Free Flow

	Proximal convoluted tubule				Distal convoluted tubule			
	Luminal diameter	Outside diameter	Length	Volume	Luminal diameter	Outside diameter	Length	Volume
	μ	μ	mm	mm^3	μ	μ	mm	mm^3
Control	25.7 ± 0.5 (n = 51)	43.8 ± 0.6 (n = 51)	10.0 ± 0.1 (n = 30)	0.097	20.2 ± 0.5 (n = 55)	31.4 ± 0.6 (n = 55)	4.6 ± 0.1 (n = 30)	0.040
Uninephrectomy	30.1 ± 0.8 (n = 42)	50.1 ± 0.9 (n = 42)	13.5 ± 0.3 (n = 30)	0.191	22.7 ± 0.6 (n = 43)	34.6 ± 0.7 (n = 43)	5.4 ± 0.1 (n = 30)	0.050
% Increase in uninephrectomized groups	17%	14%	35%	96%	12%	10%	17%	25%
P value	<0.001	<0.001	<0.001		<0.01	<0.01	<0.001	

Values represent means ± standard error. n, number of observations. Tubular diameters were measured in histological preparations of snap-frozen kidneys.

trol rats was 12.1 ± 0.4 μ and in the remaining kidney after uninephrectomy was 12.3 ± 0.4 μ. The control measurements by both methods correspond to previously reported data (14, 15). Although there are drawbacks to both methods for the determination of the actual tubular dimensions, the histological technique probably reflects more accurately the absolute value, since the brush border appears indistinct on the colored transparencies and errors due to parallax and refraction tend to diminish the measured diameter of tubules photographed on the surface of the intact kidney.

The greatest change in tubular length after compensatory growth, as reported by Oliver (16), was found in the proximal convoluted tubule. The length measured 10.0 ± 0.1 mm in control rats and 13.5 ± 0.3 mm in the experimental rats, indicating an increase of 35%. Lengthening of the distal convoluted tubule was less striking. Distal tubule length increased only 17%, from 4.6 ± 0.1 mm in the normal to 5.4 ± 0.1 mm in the hypertrophied kidneys.

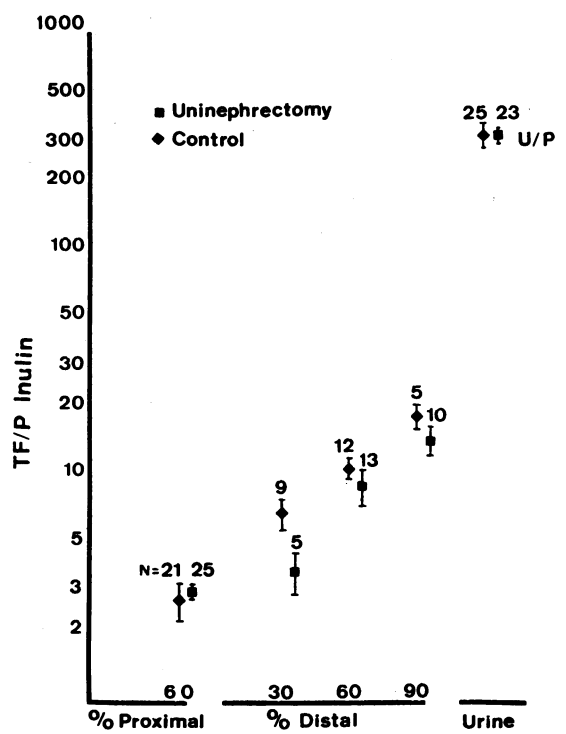

FIGURE 2 Summary of tubular fluid-to-plasma inulin concentration ratios (*TF/P*) as a function of tubular length in control and uninephrectomized rats. The mean ± standard error are represented. n, number of observations. The control and experimental values were not significantly different.

TABLE III

Reabsorption during Stopped Flow in the Proximal Tubule

	Half-time of reabsorption ($t_{\frac{1}{2}}$)	Diameter of isolated droplet	Reabsorption rate constant (*A*)
	sec	*μ*	*mm²/mm per sec*
Control	9.3±0.2 (n=48) (a=5)	35.2±0.6	7.3×10^{-5}
Uninephrectomy	9.3±0.2 (n=63) (a=6)	42.4±0.6	10.5×10^{-5}
P value	NS	<0.001	

Values represent means ± standard error. n, number of observations; a, number of animals.

Tubular volume was calculated as the product of the luminal diameter (measured in snap-frozen kidneys) and the tubular length. The volume of the proximal convoluted tubule increased 96%, while that of the distal convoluted tubule increased only 25% after compensatory growth.

Fractional reabsorption in the proximal and distal tubules. (Fig. 2). The fraction of filtered fluid which was reabsorbed in the proximal and distal tubules was similar in control and hypertrophied kidneys. The inulin TF/P in the last accessible portion of the proximal tubule, corresponding to 55–60% of its length, was 2.8 ± 0.5 (mean ± SE) in control animals and 3.1 ± 0.2 in the experimental group. Samples of tubular fluid taken along the course of the distal convoluted tubule showed a progressive increase in the inulin TF/P in both groups. Reabsorption of fluid in the collecting duct was estimated from the urine-to-plasma ratio of inulin and was also similar in both groups.

Droplet reabsorption in the proximal tubule (Table III). The reabsorption of a stationary droplet of isotonic saline in blocked tubules was studied to determine the intrinsic reabsorptive capacity of proximal tubular segments, reflected by the half-volume time ($t_{\frac{1}{2}}$). The $t_{\frac{1}{2}}$ was exactly the same in both groups, measuring 9.3 ± 0.2 sec (mean ± SE) despite a 20% ($P < 0.001$) increase in the diameter of the isolated droplet after nephrectomy.

Although the reabsorptive half-time was not changed by hypertrophy, the reabsorptive rate

TABLE IV

Reabsorption during Stopped Flow in the Distal Tubule

	Half-time of reabsorption ($t_{\frac{1}{2}}$)	Diameter of isolated droplet	Reabsorptive flux of water (J_v)
	sec	*μ*	*mm³/mm² per sec*
Control	39.3±1.7 (n=58) (a=9)	33.0±0.7	1.5×10^{-4}
Uninephrectomy	22.4±0.8 (n=39) (a=8)	35.7±0.5	2.8×10^{-4}
P value	<0.001	<0.01	

Values represent means ± standard error n, number of observations, a, number of animals.

constant was significantly increased. This rate was calculated in the manner proposed by Gertz et al. (7) in which this constant is a function of both the half-time and the square of the tubular radius.

$$A = \frac{0.693\ (r^2)}{t_{\frac{1}{2}}}, \text{ with dimensions mm}^3\text{/mm per sec.}$$

In these calculations the radius (r) was determined from the diameter of the isolated droplet which increased by 20%, from 35.2 ± 0.6 μ to 42.4 ± 0.6 μ after uninephrectomy. It should be noted that this value differs from the luminal diameter during free flow since injection of oil causes distention of the proximal tubule by approximately 50%. The reabsorptive rate constant was 7.3×10^{-5} mm³/mm per sec in normal rats and 10.5×10^{-5} mm³/mm per sec in uninephrectomized rats, an increase of 46% in the group with renal hypertrophy.

These values correspond well to those predicted from the radius during free flow, the fractional reabsorption, and the proximal transit time, when the following formula is used (7):

$$A = \frac{\ln \text{TF/P inulin } (r^2)}{\text{transit time}},$$

with dimensions mm³/mm per sec.

From these free-flow data a rate constant of 6.3×10^{-5} mm³/mm per sec was found in normal rats and 9.2×10^{-5} mm³/mm per sec in uninephrectomized rats, an increase of 44% in the group with hypertrophied kidneys.

Net reabsorptive flux of water was calculated using the formula[1]:

$$J_v = \frac{0.347r}{t_{\frac{1}{2}}}, \text{ with dimensions mm}^3\text{/mm}^2 \text{ per sec.}$$

The calculated reabsorptive flux of water was 6.5×10^{-4} mm³/mm² per sec in control rats and 7.9×10^{-4} mm³/mm² per sec after nephrectomy.

Droplet reabsorption in the distal tubule (*Table IV*). In contrast to the proximal tubule where reabsorption was increased solely as the result of an increase in tubular volume, reabsorptive capacity in the distal convolution was increased by changes in both tubular volume and half-time. Reabsorptive half-time was 39.3 ± 1.7 sec in control animals but decreased by 44% to 22.4 ± 0.8 sec after nephrectomy. The diameter of the isolated distal tubular droplet in hypertrophied kidneys was only slightly (8%) greater than in controls, indicating a minimal increase in surface area.

The calculated reabsorptive flux of water in the distal tubule showed striking changes after uninephrectomy, approximating 1.5×10^{-4} mm³/mm² per sec in control rats and 2.8×10^{-4} mm³/mm² per sec in those with one remaining kidney, an increase of 87%.

Sodium concentration in proximal and distal tubules under "steady-state" conditions (*Table V*). Because of the increase in tubular reabsorption of sodium that was demonstrated in the proximal and especially in the distal tubule after uninephrectomy, it was important to find out whether compensatory hypertrophy enhanced the capacity of the tubules to reduce the intratubular concentration of sodium under conditions of zero net flux. A droplet of isotonic solution containing raffinose, a slowly diffusing nonelectrolyte, was injected into the lumen of a tubule blocked with oil. This technique greatly reduced tubular reabsorp-

[1] Water flux (J_v) is equal to the change in volume per unit area per time t.

(*a*) $$J_v = \frac{dl(\pi r^2)}{(2\pi r l_0)dt},$$

where l_0 = length of droplet at $t = 0$, r = radius of droplet, and t = time of reabsorption.

(*b*) Integration of (*a*)

$$J_v = \ln \frac{l}{l_0} \cdot \frac{r}{2t}$$

At the time required for the reabsorption of half the volume of the saline droplet ($t_{\frac{1}{2}}$):

(*c*) $$J_v = \frac{0.693r}{2t_{\frac{1}{2}}} \text{ or } \frac{0.347r}{t_{\frac{1}{2}}} \text{ mm}^3\text{/mm}^2 \text{ per sec.}$$

TABLE V

Summary of Sodium and Potassium Values during Steady-State Conditions

	Proximal tubule			Distal tubule		
	Serum sodium	Tubular fluid sodium	TF/P	Serum sodium	Tubular fluid sodium	TF/P
	mEq/liter	*mEq/liter*		*mEq/liter*	*mEq/liter*	
Control	144.1 ± 1.5 (n = 7)	107.1 ± 1.2 (n = 38)	0.75 ± 0.01 (n = 38)	147.6 ± 0.9 (n = 8)	47.0 ± 5.4 (n = 25)	0.32 ± 0.04 (n = 25)
Uninephrectomy	146.5 ± 1.1 (n = 9)	109.8 ± 1.1 (n = 44)	0.77 ± 0.01* (n = 44)	152 ± 1.4 (n = 10)	44.8 ± 4.4 (n = 24)	0.30 ± 0.03* (n = 24)
	Proximal tubule			Distal tubule		
	Serum potassium	Tubular fluid potassium	TF/P	Serum potassium	Tubular fluid potassium	TF/P
	mEq/liter	*mEq/liter*		*mEq/liter*	*mEq/liter*	
Control	5.9 ± 0.2 (n = 7)	3.9 ± 0.2 (n = 37)	0.69 ± 0.02 (n = 37)	5.4 ± 0.2 (n = 8)	4.1 ± 0.3 (n = 25)	0.77 ± 0.05 (n = 25)
Uninephrectomy	5.9 ± 0.2 (n = 6)	3.9 ± 0.1 (n = 45)	0.66 ± 0.02* (n = 45)	5.2 ± 0.2 (n = 9)	4.3 ± 0.4 (n = 23)	0.82 ± 0.01* (n = 23)

Values represent mean ± SE. n, number of observations. TF/P, tubular fluid-to-plasma ratio.
* *P* value is not significant when compared to control.

tion of water from the drop, permitting a close approach to the steady state for rapidly permeating solutes (9). When tested in this way, TF/P for sodium was not altered by compensatory hypertrophy in either the proximal or the distal tubule. "Steady-state" concentrations of potassium were also unchanged after uninephrectomy.

DISCUSSION

Removal of one kidney from a rat stimulates prompt functional and anatomical changes in the remaining kidney. Glomerular filtration rate in that kidney rises somewhat more slowly than the increase in renal weight, but by 1 wk after uninephrectomy not only is the filtration rate per nephron increased but filtration of salt and water per gram of kidney tissue exceeds that of the normal kidney. Filtration (and reabsorption) of sodium per gram of kidney continues to increase, reaching a plateau at 2–3 wk after uninephrectomy (2). Changes in filtration rate, and presumably in tubular reabsorption, are equally rapid in human patients after unilateral nephrectomy (17).

In the present experiments, inulin clearance had increased by 92% in the remaining kidney 2–4 wk after contralateral nephrectomy. Glomerular filtration in individual cortical nephrons rose by 75%. Because of this increase in filtration rate, tubular reabsorption of sodium must be augmented in compensatory hypertrophy. Changes in tubular diameter are of special interest when we consider the mechanism of accelerated tubular reabsorption, since it is possible that proximal tubular absorption of sodium is directly influenced by passive changes in tubular diameter or circumference (18). The average diameter of proximal tubules increased by 17% in the present study, when measured by the quick freezing technique during free flow. The changes in luminal diameter in the proximal tubule are of the same order of magnitude as those seen after rapid saline infusion. After saline loading, however, tubular reabsorption is diminished, rather than increased. An important difference between the tubular dilatation of compensatory hypertrophy and that of saline diuresis is that in the former, the peritubular or antiluminal circumference as well as the luminal circumference is increased, whereas during saline infusion, the cells are greatly flattened so that although the tubular lumen is widened, the peritubular circumferance is not expanded. Since in the process of tubular reabsorption sodium is actively pumped from the basal

or peritubular end of the cell, these differences may be relevant to the differences in functional behavior between the dilated proximal tubule of compensatory hypertrophy and the dilated proximal tubule of saline diuresis.

It appears from the present data that the proportion of glomerular filtrate reabsorbed in the proximal and distal tubules is roughly the same in hypertrophied as in normal kidneys. The mechanism of this increased reabsorption, however, differs in the proximal and distal tubules. These differences may be related to the anatomical changes produced by hypertrophy. Anatomical studies of hypertrophied kidneys show that the bulk of the increase in renal mass is due to an increase in length and width of the proximal tubule. The pars recta and loop of Henle are also elongated. In the present experiments transit time through the proximal tubule was not affected by compensatory hypertrophy, indicating that the increase in proximal tubular volume was roughly proportional to the increase in proximal tubular flow. The prolongation of time taken for dye to pass to the distal tubules suggests that, stimulated by hypertrophy, elongation of the pars recta and of Henle's loop was disproportionate to the flow of urine through these segments of the tubule.

The distal tubule hypertrophies least of all the segments of the nephron when the opposite kidney is removed. Luminal diameter of the distal tubule was hardly changed when measured during free flow by the quick freezing technique and by photographing dye-filled tubules on the surface of the kidney, or during stopped-flow by the split-droplet method. Nevertheless, the distal tubule reabsorbs increased quantities of sodium and water. This increased reabsorption is reflected in an increased reabsorptive capacity per segment of tubule, as measured by the shrinking-droplet technique of Gertz. Reabsorptive half-time of a droplet of saline in the distal tubule averaged only 22.4 sec after uninephrectomy compared with 39.3 sec in control rats. It is difficult to translate this finding precisely into differences in the rate of transport of sodium, since the concentration of sodium in the droplet was not measured after it was injected into the tubule. The concentration of sodium in an isolated droplet of saline in the distal tubule was reported by Malnic, Klose, and Giebisch to vary from 66 to 89% of plasma sodium (19). It seems likely that the net rate of sodium reabsorption from oil-blocked distal tubules rose anywhere from 30 to 150% during compensatory hypertrophy.

An increase in the active transport of sodium by tubular cells suggests an increase in the strength of the sodium pump. This might be reflected in a fall in the steady-state concentration of sodium in an isolated raffinose drop. In the stationary microperfsuion experiments, however, such a fall was found after uninephrectomy in neither the proximal nor the distal convolution, even though reabsorption of the saline droplet *without* raffinose by the distal tubule was greatly accelerated. A formal explanation of this interesting combination of findings would require the accurate measurement of transtubular potentials and ionic fluxes in the raffinose and saline droplets. It is as if the capacity of the sodium pump, expressed in milliequivalents per unit of tubular length per minute, were increased without a change in the critical energy barrier against which sodium is pumped. One explanation might be that the permeabilities of tubular membranes to water and sodium were changed by compensatory hypertrophy. Another possible explanation is that the number of "sodium pumps" per unit length in the distal tubule was increased, but that they were placed in parallel positions rather than in series. This phenomenon might occur if the basal infoldings of distal tubular cells (where pumping of sodium is thought to take place) were multiplied in the course of compensatory hypertrophy.

The increase in distal reabsorption after nephrectomy is reminiscent of that noted after acute expansion of the extracellular fluid, when the half-time of droplet resorption by the distal tubule is also greatly diminished (13). The mechanism is not likely to involve a simple response to the delivery of more fluid into the distal from the proximal tubule, since the phenomenon is apparent in distal tubular segments isolated by columns of oil from other parts of the nephron. It is interesting that after subtotal nephrectomy in dogs free water clearance per GFR is increased, which implies an increased rate of sodium reabsorption in the ascending loop of Henle and distal convoluted tubule (20).

The increase in net reabsorption per unit length and surface in proximal and distal tubules demon-

strated in these experiments suggests that the active transport of sodium per unit of cell membrane may also be increased. A biochemical explanation for this functional change may perhaps be found in the increased activity of Na-K-ATPase induced in kidney microsomes by compensatory renal hypertrophy (21).

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