Increased Ureteral Back Pressure Enhances Renal Tubular Sodium Reabsorption

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ABSTRACT Moderate increases of ureteral back pressure usually cause decreases of glomerular filtration rate and even greater decreases of sodium excretion. It has been assumed previously that increased ureteral back pressure does not enhance renal tubular sodium reabsorption directly and that the decreases of sodium excretion are caused by the decreases of glomerular filtration rate. In the experiments reported here, the effect of increased ureteral back pressure on urinary sodium excretion was studied in dogs in which changes of filtration rate were minimized by infusing saline while ureteral back-pressure was increased.

When ureteral back pressure was increased on one side by 10–23 cm of water, the inulin clearance of the experimental kidney decreased by only 3–12% in 21 experiments, did not change significantly (±2%) in eight experiments, and increased by 3–8% in seven experiments. The sodium excretion of the experimental kidney decreased in *all* experiments regardless of whether its inulin clearance increased, decreased, or was unchanged from control values.

When the inulin clearance of the experimental kidney increased or remained unchanged during increased ureteral back pressure, its reabsorption of sodium increased more than could be accounted for by the increase of filtered sodium. When the inulin clearance of the experimental kidney decreased during increased ureteral back pressure, its reabsorption of sodium decreased less than could be accounted for by the decrease of filtered sodium.

Therefore, the effect of increased ureteral back pressure to decrease urinary sodium excretion is caused in part by increased tubular reabsorption of sodium.

INTRODUCTION

Acute increases of ureteral back pressure in dogs usually cause decreases of glomerular filtration rate (GFR) and disproportionately larger decreases of sodium excretion (1–3). It has been assumed that the decrease of sodium excretion ($U_{Na}V$) is secondary to the decrease of GFR and that increased ureteral back pressure does not enhance tubular sodium reabsorption directly (2). The present study was directed toward the question of whether increased ureteral back pressure might have a direct effect on the renal tubular reabsorption of sodium, independent of any decrease of GFR.

Whereas moderate increases of ureteral back pressure (25–40 cm of water) usually cause GFR to decrease (1–3), infusions of 145 mM NaCl (saline) tend to increase the GFR in dogs (4). Lesser elevations of ureteral pressure in dogs that are given moderately large infusions of saline may not cause GFR to decrease but may serve only to minimize the saline-induced increase. In such dogs, the GFR may remain unchanged or even continue to increase above control values. We found that under these conditions sodium excretion nevertheless still decreased. Such decreases of $U_{Na}V$ could not be attributed to decreased GFR and, therefore, must have resulted from increased tubular reabsorption of sodium.

METHODS

The experiments were performed in 22 mongrel female dogs (13.5–22.0 kg, average 18.2 kg) that were deprived of food and water for 18 hr before they were anesthetized with pentobarbital, 30 mg/kg administered intravenously. Light anesthesia was maintained with small supplemental doses of pentobarbital. Four dogs were given 1–2 mU/kg per min of aqueous pitressin throughout the experiment. Six other dogs were given deoxycorticosterone (DOC), 10 mg in oil, intramuscularly 18 hr before the experiment and again at its start. Three of the DOC-treated dogs were also given intramuscularly 2.5 U of pitressin in oil 18 hr before the experiment and again at its start.

The dogs lay supine throughout the experiment, and both ureters were isolated through a midline suprapubic incision and then cannulated supravesically with PE tubing that was usually advanced to about 3–4 cm above the bladder. They were rapidly given, first, 200–300 ml of saline intravenously, then the appropriate priming solutions, and then 0.5 ml/kg

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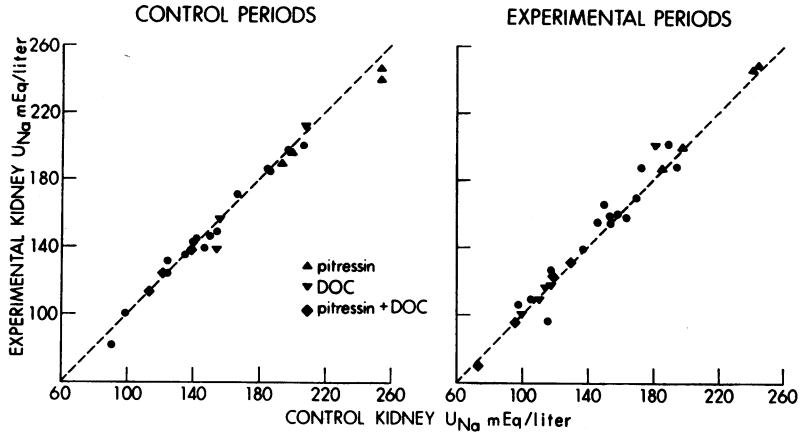

FIGURE 1 Comparison of sodium concentrations in urines from the two kidneys of dogs receiving infusions of isotonic saline. Left, control periods; right, experimental periods. ▲, pitressin-treated dogs; ▼, DOC-treated; ◆, pitressin-plus-DOC-treated. The dashed line is the 45° line of identity.

per min of 145 mM NaCl with inulin (and in five cases, creatinine). The sustaining infusions were given for 60–230 min (average 114 min) before starting separate urine collections from each kidney. Control collections consisted of two to four (average 2.8) consecutive 10-min (or occasionally 8-min) periods in which the volumes (V) usually matched very closely. Midpoint jugular venous blood was taken in heparinized syringes in 15 dogs, and carotid arterial blood was taken in the others. GFR was estimated by the clearance of inulin (C_{In}) in all experiments and was confirmed by the clearance of exogenous creatinine (C_{Cr}) in five. The equilibration periods were sufficiently long so that the plasma concentrations of inulin (P_{In}, 21.1–45.0 mg/100 ml, average 34.7) and of creatinine (P_{Cr}, 21.5–32.6 mg/100 ml, average 28.2) remained very stable throughout each experiment, as did P_{Na}. In six experiments (including the five in which creatinine was given) the concentration of Cl in plasma and urine was measured along with that of Na.

By the time control clearance collections were started, the total urinary flow was in approximate volume equilibrium with the infusion in all but four dogs. Although those four had "normal" GFR's and had not received pitressin, their urinary flow rates remained only about one-half their infusion rates throughout the control periods.

In the choice of which kidney would be "obstructed," preference was usually given the one that had the slightly higher control flow. After the control measurements, one catheter was elevated, and the subsequent clearance periods are designated "obstruction" or "experimental." The magnitude of ureteral back pressure is reported in terms of centimeters of elevation of the catheter tip above the *table*. The actual increases of ureteral back pressure were about 4–5 cm less than those reported because the animals' renal pelves were above the table. In the 14 earlier experiments the initial pressure elevation was between 15.0 and 23.0 cm of water (average 19.4 cm); in the 11 later experiments the range was 10.0–16.5 cm (average 13.8 cm). In preliminary studies, similar pressure elevations had been found to cause V decreases of about 10% from control flow rates, with relatively little change of C_{In}. Experimental period urine collections were usually not started until at least 10–15 min after the pressure was elevated, thereby permitting the discard of at least 25 ml of urine from each kidney. The adequacy of the discard periods may be judged from the fact that the concentration of P_{In} remained virtually unchanged during the subsequent obstruction periods. Urine was then collected from each kidney for two to three (average 2.6) consecutive 8–10-min periods, and in eight dogs the study was then ended. In eight other dogs the catheter elevation was changed by −2.0 to +7.5 cm (average +3.1 cm), and another group of two to three consecutive clearance periods was obtained from each kidney after a comparable discard period. In three other dogs, the original pressure elevation was maintained, and a further set of clearance measurements was made during the infusion of additional saline at a rate of 1.3–4.4 ml/min. Finally, in three other dogs, the elevated catheter was returned to table level and, after a suitable discard period, another set of control clearance periods was obtained, after which the catheter of the previous control kidney was elevated, and a final set of obstruction periods was obtained. The data from the second set of periods in the latter six dogs are recorded as separate experiments, thereby yielding 28 sets of "first-level obstruction" data and eight sets of "second-level obstruction" data from the 22 dogs.

The results are reported as the averages for per minute excretion (UV), clearance (C), filtered load (F), and tubular reabsorption (T) obtained for each kidney during the groups of closely matched consecutive periods. The filtered load of Na was calculated as the concentration of plasma Na × C_{In} × a Donnan factor of 0.94. Tubular reabsorption was calculated as $F_{Na} - U_{Na}V$. The control kidney periods are designated as C1 for control periods and C2 for experimental periods. The experimental kidney periods are designated similarly as E1 and E2. Statistical calculations were made with standard methods using Student's t test (5).

All chemical analyses were performed at least in duplicate, using methods reported previously from this laboratory (6, 7).

RESULTS

Urinary flow and sodium excretion. The flow of urine from the experimental kidney decreased promptly

after catheter elevation, and this was always associated with a proportionate or even greater decrease of sodium excretion. Urinary sodium concentration (U_{Na}) was very similar on both sides during concurrent periods (Fig. 1) and either remained the same or else decreased somewhat on *both* sides during obstruction. The "preobstruction" mean U_{Na} for the experimental kidney was 158.8 mEq/liter ±7.8 (SE), and its first-level obstruction mean was 157.3 mEq/liter ±8.3. While the urinary flow and $U_{Na}V$ of the experimental kidney always decreased during obstruction, $U_{Na}V$ of the control kidney meanwhile increased over its control values in 12 experiments and remained stable in four. In the other 12 experiments $U_{Na}V$ decreased on *both* sides during first-level obstruction, though more markedly on the experimental side (*v.i.*).

When the elevated catheter was returned to table level after the obstruction period urine collections were completed, the experimental kidney urinary flow usually increased promptly. In the three experiments in which measurements were then repeated, the ratios of experimental/control kidney V, $U_{Na}V$, and C_{Na}/C_{In} returned toward those of the original control periods, as also observed by Selkurt, Brandfonbrener, and Geller (*2*).

During increased ureteral back pressure, the inulin clearance of the experimental kidney *increased* by 3–8% in seven experiments and did not change significantly (±2%) from control values in eight experiments. In the other dogs, the experimental kidney C_{In} decreased by 3–12% from control values although the increases of ureteral back pressure were similar. These decreases of C_{In} may not have been attributable *entirely* to the pressure elevation because the control kidney C_{In} often decreased also, though less. These dogs usually also had bilateral decreases of sodium excretion during the experimental periods, invariably greater on the obstructed side, however. The bilateral decreases of $U_{Na}V$ (and perhaps also of GFR) were probably attributable to the tendency of saline diuresis not to be sustained stably, but rather to wax and wane. That is, in some experiments, ureteral pressure was raised while $U_{Na}V$ happened to be stable or increasing, and in others, the periods of increased back pressure happened to coincide with a recession of saliuresis from its peak values.[1]

Table I shows the mean values for F_{Na}, $U_{Na}V$, and T_{Na} for both kidneys during the control and the experimental periods in all of the experiments except dog No. 22.[2] The decrease of sodium excretion by the experimental kidney might appear related to the decrease of F_{Na}, and presumably, this was a factor in the experiments where C_{In} decreased moderately during obstruction. However, the values in those experiments weighted the averages heavily, thereby obscuring the increase of experimental kidney T_{Na} that occurred in the experiments in which C_{In} did not decrease (Figs. 2 and 3). Accordingly, it is much more informative to examine the data in the experiments where C_{In} increased or remained unchanged during obstruction.

Table II shows the mean values for F_{Na}, $U_{Na}V$, and T_{Na} in the 13 of 15 experiments[3] in which the experimental kidney C_{In} increased while ureteral back pressure was increased. In the control kidneys, the mean increases of F_{Na} and of T_{Na} were almost identical, and mean U_{Na}

[1] We cannot exclude the possibility that the bilateral decreases of $U_{Na}V$ were secondary to the unilateral elevation of ureteral pressure, but we think this is unlikely, as did Share (1).

[2] The experimental and the control kidneys in dog No. 22 had unequal C_{In} values (42.9 and 69.8 ml/min) and unequal weights (35 and 75 gm), but both kidneys appeared otherwise normal when examined at the end of the experiment.

[3] The data for dog No. 22 are omitted; see footnote 2.

TABLE I

*Mean Values for Filtered Sodium, Urinary Sodium Excretion, and Tubular Sodium Reabsorption before and after Increased Ureteral Back Pressure in 34 Experiments**

Kidney	Observation period	F_{Na}	$U_{Na}V$	T_{Na}
		μEq/min	*μEq/min*	*μEq/min*
Control	Control (C1)	5601 ±185	549 ±32	5052 ±178
	Experimental (C2)	5615 ±196	523 ±26	5091 ±194
	Δ(C2 − C1)	+14 ±58	−26 ±18	+40 ±53
Experimental	Control (E1)	5724 ±180	607 ±32	5116 ±177
	Experimental (E2)	5543 ±182	466 ±23	5077 ±184
	Δ(E2 − E1)	−181 ±60	−146 ±15	−30 ±54
P value for difference between mean Δ(E2 − E1) and mean Δ(C2 − C1)		< 0.025	< 0.001	> 0.3

F_{Na}, filtered sodium; $U_{Na}V$, urinary sodium excretion; T_{Na}, tubular sodium reabsorption.

* Excluding dog No. 22 (see footnote 2 in text). Values are given as the mean ±SE.

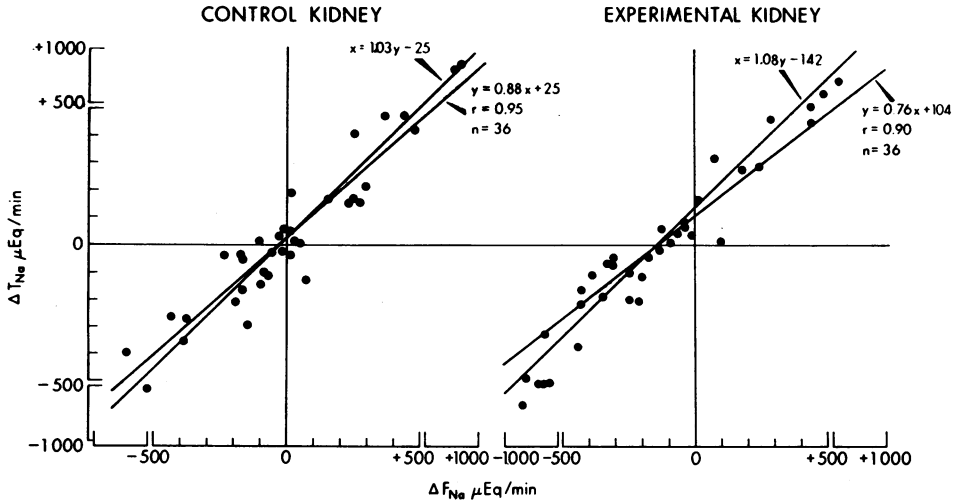

FIGURE 2 Experimental period minus control period values of tubular reabsorption (T_{Na}) and filtered load (F_{Na}) of sodium for the control (left) and the experimental (right) kidneys. The experimental periods were obtained while the experimental kidney was subjected to increased ureteral back pressure.

remained unchanged. In the experimental kidneys, the mean increase of F_{Na} was only one-half of that in the control kidneys because GFR did not increase as much. In contrast to the control kidneys, the increase of T_{Na} in the experimental kidneys considerably exceeded the increase of F_{Na} so that mean $U_{Na}V$ decreased. Note also that the mean increases of T_{Na} were very similar in the experimental and in the control kidneys despite their disparate changes of F_{Na}.

Thus, in the control kidneys, the average changes of

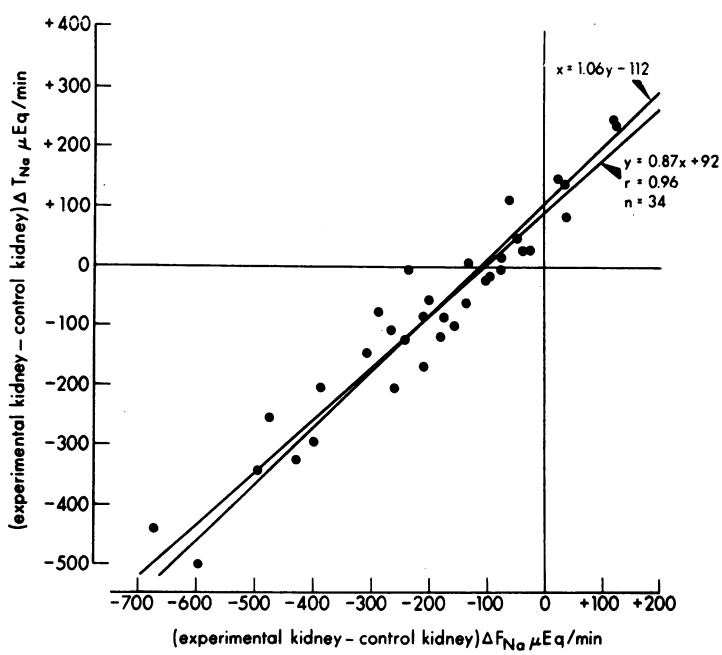

FIGURE 3 The relation between the changes of tubular sodium reabsorption (T_{Na}) and filtered load (F_{Na}) of sodium. The data are given in terms of the *differences* between the experimental and control periods in each kidney, ([E2 − E1] − [C2 − C1]) (see text). The data from dog No. 22 with unequal-sized kidneys are not included (see footnote 2 in text).

TABLE II

*Mean Values for Filtered Sodium, Urinary Sodium Excretion, and Tubular Sodium Reabsorption before and after Increased Ureteral Back Pressure in 13 Experiments with Stable or Increasing Glomerular Filtration Rate**

Kidney	Observation period	F_{Na}	$U_{Na}V$	T_{Na}
		μEq/min	*μEq/min*	*μEq/min*
Control	Control (C1)	5457 ±265	505 ±50	4951 ±268
	Experimental (C2)	5738 ±309	495 ±51	5243 ±312
	Δ(C2 − C1)	+281 ±88	−10 ±20	+291 ±86
Experimental	Control (E1)	5543 ±237	564 ±54	4979 ±253
	Experimental (E2)	5685 ±265	449 ±45	5236 ±279
	Δ(E2 − E1)	+142 ±67	−114 ±18	+257 ±66
P value for difference between mean Δ(E2 − E1) and mean Δ		< 0.025	< 0.001	> 0.3

* Experimental kidney C_{In} increased by 3–8% over its control period values in six experiments and was ±2% of its control period values in seven experiments during increased ureteral back pressure.

T_{Na} were very similar to the changes of F_{Na}. In the experimental kidneys, in contrast, T_{Na} increased disproportionately more than F_{Na} when GFR increased or remained stable; and, in the other experiments, T_{Na} decreased less than expected from the decrease of F_{Na}. A graphic analysis of the differing behavior of the two kidneys is informative. Fig. 2 (left) shows the changes (Δ) of T_{Na} and F_{Na} in the control kidney between the experimental and control periods (C2 − C1). The relation between T_{Na} and F_{Na} is essentially linear, and the slopes of the regression lines are close to 1.0 because most of the filtered sodium was reabsorbed. Another feature is particularly noteworthy; the y-intercept values (+ 24 and + 25 μEq/min) do not differ significantly from zero ($P > 0.1$). In contrast, in the experimental kidney (Fig. 2, right), the y-intercept values (+ 104 and + 132 μEq/min) differ very significantly from zero ($P < 0.001$). That is, unlike the control kidney, when the experimental kidney F_{Na} did not change between the control and the experimental periods (i.e., $x = 0$), T_{Na} was greater during obstruction than during the control periods. Moreover, the experimental kidney ΔT_{Na} invariably exceeded ΔF_{Na} (or was "less negative") in all the experiments, whereas in the control kidney $\Delta T_{Na} \sim \Delta F_{Na}$.

The differing T_{Na} behavior of the two kidneys is emphasized in Fig. 3 which shows the *difference* between the changes of T_{Na} and F_{Na} in the two kidneys of each dog between the experimental and control periods, ([E2 − E1] − [C2 − C1]) which is arithmetically the same as ([E2 − C2] − [E1 − C1]). When $x = 0$, $y = +92$ and + 106 μEq/min for the two regression lines. That is, in the ideal circumstance that the F_{Na} changes between the experimental and the control periods were the same in both kidnys (i.e., GFR did not change or else changed equally), the experimental kidney increased its tubular reabsorption of sodium during obstruction ($P < 0.001$). This effect of increased ureteral back pressure to increase T_{Na} was independent of whether DOC or pitressin was given, and in the experiments in which creatinine and chloride measurements were made, those data agreed closely with the inulin and sodium data.

Potassium excretion. Urinary potassium concentrations (U_K) were virtually the same on both sides during the control periods, averaging 15.0 mEq/liter ±0.9 (SE) for the control kidney and 14.3 mEq/liter ±0.8 for the experimental kidney. Following ureteral pressure elevation, mean U_K increased slightly on both sides, to 15.3 mEq/liter ±1.0 for the control kidney and somewhat more, to 16.6 mEq/liter ±1.2, for the experimental kidney. The difference between the mean changes of U_K on the two sides was statistically significant but trifling, + 0.3 mEq/liter ±0.6 for the control kidney and + 2.3 mEq/liter ±0.6 for the experimental kidney ($P < 0.025$). The increase of experimental kidney U_K just sufficed to maintain U_KV near its average control period values of 55 μEq/min.

DISCUSSION

The importance of glomerular filtration rate (8) and aldosterone activity (9) in the control of renal sodium excretion has been well documented (reviewed in 10–15), but it is recognized that other factors are probably also involved (13–16). It has been suggested, for example, that increased renal venous pressure might enhance tubular sodium reabsorption (17, 18) and, on the other hand, that there might be a natriuretic hormone of adrenal or other origin (11, 13, 14, 16). More recently,

deWardener, Mills, Clapham, and Hayter (19) and others (20–25) have shown that there must also be other major factor(s) controlling the fractional reabsorption of sodium. Whether the "third factor" is hormonal (13, 26–28) or is the result of alterations in intrarenal physical parameters (15, 23, 29–31) has yet to be determined.

The remarkable *anti*natriuretic effect of increased ureteral back pressure was emphasized by Share (1) and by Selkurt, Brandfonbrener, and Geller (2) and has been confirmed by us (3). With increases of pressure larger than those used here GFR usually decreased, and so it was inferred that the GFR decrease somehow caused the decreased $U_{Na}V$ that followed ureteral pressure elevation (2). The possibility that this might not be the entire explanation arose during experiments on the effect of increased ureteral back pressure on the excretion of urea (3). In one experiment, performed during the infusion of 0.4 ml/kg per min of 145 mM NaCl with 10 mg/ml urea, increased ureteral back pressure was accompanied by an *increase* of the obstructed kidney's C_{In} from 44.5 to 48.2 ml/min, despite which $N_{Na}V$ decreased from 331 to 164 μEq/min. Meanwhile, C_{In} of the control kidney increased from 47.0 to 52.3 ml/min, and its $U_{Na}V$ increased from 313 to 351 μEq/min. It seemed possible that this unexpected finding could be explained by the known tendency of saline infusion to increase GFR, an effect that was dampened only partially by the increased ureteral back pressure. If so, the observed decrease of $U_{Na}V$ must have been caused by increased ureteral back pressure enhancing tubular sodium reabsorption independent of its effect on GFR. The present study was an attempt to examine this possibility in dogs given saline without urea.

Ideally, one would prefer experiments that fulfill the following two criteria: *first,* that the GFRs of both kidneys should remain constant or at least change equally during the study, and *second,* that the control kidney $U_{Na}V$ should remain constant when the other kidney was obstructed. In the dogs in which these criteria were approximated, i.e. about one-half of the series, the obstructed kidney excreted less sodium than the control kidney under circumstances that their respective GFR behavior could not account for the difference (Table II). Moreover, when suitable mathematical corrections were made for (*a*) the relative F_{Na} behavior of the two kidneys and (*b*) the over-all natriuretic trend in each experiment, the same effect of increased ureteral back pressure to enhance tubular sodium reabsorption was evident in *all* of the experiments (Figs. 2 and 3). Share had also suggested this possibility by noting in some of his experiments that, despite an increase of C_{Cr} toward control values during the second of paired obstruction periods, $U_{Na}V$ nevertheless remained below control values (Table I) (1).

The procedural, technical, and analytical problems that can complicate the interpretation of studies of renal sodium excretion in relation to GFR changes have been discussed by Wesson (10). Most of those difficulties have been controlled, minimized, or even eliminated here in the following ways: (*a*) the equilibration periods were relatively long, and so P_{In} concentrations remained very stable during consecutive clearance periods; (*b*) the high rates of ureteral urine flow minimized the dead-space factor; (*c*) the discard periods were generous and P_{In} concentrations were again very stable during the subsequent obstruction periods; (*d*) in five of the experiments the inulin and sodium results were confirmed closely by creatinine and chloride measurements.

The difficulty of ascribing physiologic significance to small changes of C_{In} is well known (10). Nevertheless, the increases of C_{In} observed in seven of the experiments were compatible with the known GFR-enhancing effect of saline infusion (4). Moreover, because the obstructed kidney was always compared simultaneously with the control kidney, the effect of any errors of blood chemical analysis or blood collection timing were obviated.

The data do not indicate how increased ureteral back pressure increases tubular sodium reabsorption independent of GFR changes. Saline loading was used here to offset the GFR-depressing effect of increased ureteral back pressure. However, saline loading also influences T_{Na} (19–24), perhaps partly through hemodynamic changes (29–31). Therefore, it is possible that the mechanism by which increased ureteral back pressure enhances T_{Na} is by inhibiting the decrease of fractional Na reabsorption caused by saline loading.

The antinatriuretic effect of increased back pressure might involve a neural circuit in which the ureter or pelvis might participate as a sensor. It is possible that it is not the increased *ureteral* pressure per se that is the proximate physical cause of the increased tubular sodium reabsorption, but that the critical site of pressure change is intrarenal (32). Blake, Wegria, Keating, and Ward suggested that increased renal venous pressure caused increased tubular reabsorption of sodium independent of significant changes of GFR (17). Their conclusions have been questioned on technical grounds (18), but their hypothesis may be correct and perhaps relevant to the present observations.

It is conceivable that increased ureteral back pressure may have caused changes of renal blood flow that were responsible for the increases of sodium reabsorption. Effective renal plasma flow was not measured in these experiments but very likely did not decrease much. Share (1) and Selkurt, Brandfonbrener, and Geller (2) found that the clearance of para-aminohippurate (C_{PAH}) usually decreased less than did C_{Cr}, and sometimes it in-

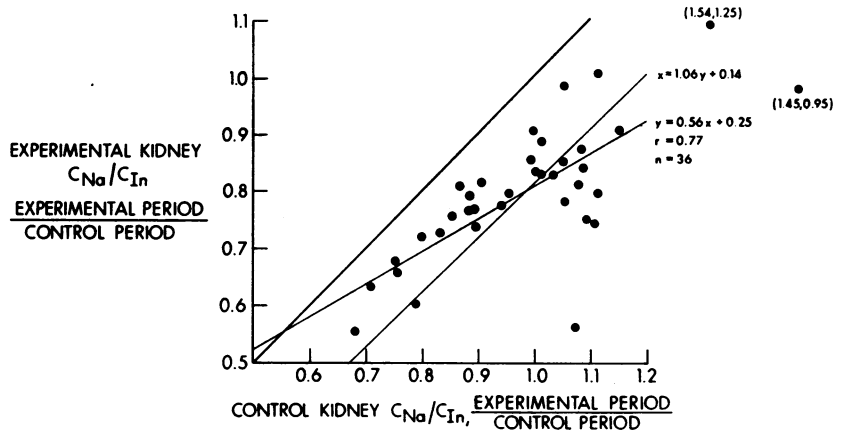

FIGURE 4 A comparison between the C_{Na}/C_{In} of the experimental kidney and the control kidney before and during increased ureteral back pressure. The clearance ratios are presented in terms of the respective values for experimental/control periods, i.e., E2/E1 and C2/C1. The 45° line of identity is shown.

creased even though C_{Cr} decreased modestly during increased ureteral back pressure. Of course, obstruction may cause changes of *medullary* blood flow that might not be reflected by changes of C_{PAH}.

The site of the increased tubular sodium reabsorption caused by increased ureteral back pressure is uncertain but may be a rather distal part of the tubule because in most of these experiments the actual pressure increments were no higher than about 15 cm of water, and often lower. The data available in the literature do not permit any inferences about how far up the tubule such small pressure increments might be transmitted (33, 34). Moreover, recent proximal tubular micropuncture observations made in saliuretic rats subjected to even higher levels of ureteral back pressure suggest that fractional sodium reabsorption in the proximal tubule did not change under those conditions (35, 36).

That neither DOC nor pitressin affected the results makes it unlikely that they are involved other than permissively, but angiotensin or prostaglandins might be. Vander (37) and others (38) have suggested that angiotensin II may inhibit distal tubular sodium reabsorption directly. If so (although Burg and Orloff [39] found that angiotensin did not affect proximal tubular sodium reabsorption), increased ureteral back pressure might affect the juxtaglomerular apparatus to inhibit the secretion of angiotensin II and thereby permit increased distal tubular reabsorption of sodium.

In speculating about the possible physiologic and clinical significance of these findings, one must remember that the experiments involved acute increases of ureteral pressure during saline infusion. If the phenomenon has a chronic counterpart in humans, it may be relevant to the pathogenesis of some clinical states of chronic sodium retention, for example, the edema that can occur during pregnancy in otherwise healthy women.

APPENDIX

The lack of perfect stability of GFR and $U_{Na}V$ in saline-infused dogs means that one cannot compare just the obstruction period values of the experimental kidney (E2) with *its* earlier control period values (E1). On the other hand, if the control period values for the experimental (E1) and the control kidney (C1) are not *identical,* it is also not adequate to compare just the obstruction period values of the experimental kidney (E2) with the concurrent values of the control kidney (C2). It is necessary, therefore, to take into account the GFR and sodium excretion behavior of (*a*) both kidneys during obstruction and (*b*) the earlier relation of those two measurements for both kidneys during the control periods.

This can be accomplished in either of two ways. In the text, the data were normalized by comparing the differences of absolute F_{Na}, $U_{Na}V$, and T_{Na} values for the two kidneys (Tables I and II and Figs. 2 and 3). The other way of normalizing the data is by comparing the *relative* changes of clearance or excretion values for the two kidneys as *ratios.* This approach has the advantages that all values for (*a*) urinary volume and (*b*) plasma concentrations of both inulin and sodium disappear from the final formula because the identical values appear in both numerator and denominator and hence cancel. Thus, we can compare the experimental and the control kidneys with respect to their experimental/control period values of C_{Na}/C_{In} (Fig. 4); that is, the ratio of C_{Na}/C_{In} for E2/E1 (ordinate) compared with C2/C1 (abscissa). The final formula for the slope of the regression equation is:

$$\frac{U_{Na_{E2}} \cdot U_{Na_{C1}}}{U_{Na_{C2}} \cdot U_{Na_{E1}}} \times \frac{U_{In_{E1}} \cdot U_{In_{C2}}}{U_{In_{E2}} \cdot U_{In_{C1}}} \qquad (1)$$

Incidentally, because both kidneys had virtually the same U_{Na} during concurrent periods (Fig. 1), the formula can be simplified further to one that contains only values of

urinary inulin concentration, although this is not how the actual calculations were made:

$$\frac{U_{In_{E1}} \cdot U_{In_{C2}}}{U_{In_{E2}} \cdot U_{In_{C1}}} \quad (2)$$

The value of particular interest is that for E2/E1 in the ideal circumstance that the control kidney C_{Na}/C_{In} was constant throughout; that is, when C2 = C1 and hence, in Fig. 4, when $x = 1.00$. Then, $y = 0.81$, which means that when the C_{Na}/C_{In} of the control kidney was constant, the experimental kidney C_{Na}/C_{In} during obstruction averaged 81% of *its* preobstruction value.

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