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J Clin Invest. 1966;[45\(1\)](#):122-131. <https://doi.org/10.1172/JCI105316>.

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Patterns of Nephron Perfusion in Acute and Chronic Hydronephrosis *

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Partial urinary tract obstruction is known to produce, in addition to a nonspecific depression in renal function, certain characteristic derangements, especially profound polyuria (1-5); release of the obstruction may result in a transient salt-wasting state (6, 7). Three hypotheses may be advanced to explain the altered function of the hydronephrotic kidney. It is possible that with the elevation of intrapelvic pressure a significant fraction of the nephron mass stops functioning, due either to mechanical damage or cessation of filtration, whereas the remaining nephrons continue to function with decreased tubular flow. This decreased rate of tubular flow could be due to reduced filtration per nephron or increased proximal fractional reabsorption, or both. This hypothesis would imply a reduced delivery of filtrate to the loop of Henle and the distal convoluted tubule and would, therefore, result in a pattern of nephron underperfusion (8). An alternative possibility is that the initially elevated intrapelvic pressure results in a reduction in nephron mass; the subsequent return of intrapelvic pressure towards normal might produce a compensatory increase in the rate of tubular flow in the residual nephrons (9). The increased rate of tubular flow could result from increased filtration per nephron or diminished proximal fractional reabsorption, or both. The increased tubular flow per nephron increases the

delivery of filtrate to the distal nephron resulting in overperfusion of that portion. Finally, varying degrees of nephron damage might be superimposed on either of the two patterns of nephron perfusion. No studies are available to determine which of these theoretical considerations best fits the observed disorders of renal function.

This study was undertaken, therefore, to clarify the pattern of renal function in hydronephrosis. The excretion of salt and water during water and hypotonic saline diuresis was examined in dogs with either acute or chronic unilateral hydronephrosis; the contralateral kidney served as an internal control. The results from these two models of hydronephrosis were compared to those from an experimental model known to result in nephron underperfusion, namely, renal arterial constriction (8).

Methods

The effects of acute and chronic hydronephrosis and of renal arterial constriction were studied in 14 female mongrel dogs weighing 8 to 15 kg and fed commercial diets. A total of 22 studies was performed during water diuresis followed by hypotonic saline diuresis.

Water diuresis was induced by the administration of 50 ml of water per kg body wt via a gastric tube and maintained by the intravenous infusion of 2.5% solution of dextrose in distilled water at a rate of 10 ml per minute. When the water diuresis was well established, two or three urine and blood collections were made. Hypotonic saline solution (0.45 to 0.58%) was then started at a rate of 20 ml per minute, and 30 to 45 minutes later two or three more urine and blood collections were made. After the termination of the urine collections during hypotonic saline diuresis, the maximal tubular transport rate for *p*-aminohippurate (T_{mPAH}) was measured in four experiments during acute hydronephrosis and four experiments during chronic hydronephrosis by the infusion of loading and maintenance doses of PAH sufficient to produce a plasma level of 11 to 30 mg per 100 ml. This insured a load to T_m ratio of at least 2 to 3, even in the presence of marked reductions in renal blood flow (10).

* Submitted for publication August 19, 1965; accepted October 13, 1965.

Supported in part by grants I-SOI-FR 5426 and 5TI HE-5469 from the National Institutes of Health, U. S. Public Health Service.

Presented in part at the National Meeting of the American Society for Clinical Investigation on May 2, 1965; a preliminary report appeared in *J. clin. Invest.* 1965, **44**, 1103.

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Acute hydronephrosis was induced in seven dogs by the elevation to variable levels (60 to 80 cm H₂O) of a polyethylene tube inserted in the left ureter. The animals were first anesthetized with 30 mg per kg pentobarbital intravenously, and then through a midline abdominal incision each ureter was cannulated with a polyethylene tube reaching into the renal pelvis.

The renal artery was constricted in four anesthetized animals. Through a left flank incision, a silk tie was placed around the left renal artery, which was constricted sufficiently to reduce blood pressure distal to the constriction by 50%. The blood pressure was monitored by a small needle in the renal artery distal to the point of constriction, connected to a Statham strain gauge and a Sanborn recorder. Both ureters were cannulated with polyethylene tubing.

In six dogs a bladder-splitting operation was first performed to permit the collection of urine from each kidney separately (11). Nine to 12 days later a control study was performed to ascertain whether glomerular filtration rate (GFR), sodium excretion, and free water clearance (C_{H_2O}) were equal on the two sides. Through a paramedian abdominal incision the left ureter was then exposed and a silk tie placed around it, partially occluding it in the region of the ureteropelvic junction. In one dog the induction of chronic hydronephrosis was preceded by the cannulation of the left ureter and a study of acute hydronephrosis. These chronically hydronephrotic animals were then studied 7 to 124 days after the constriction of the ureter.

The GFR was measured by the clearance of inulin. Inulin, PAH, sodium, potassium, and urinary solute concentrations were measured by previously published methods (8). The data were analyzed by a nonparametric median test (12).

Results

Figure 1, constructed from our previously published data (8), depicts the effects of acute renal arterial constriction. During water diuresis GFR, urinary flow, and urinary sodium concentration (U_{Na}) were always lower, and total solute concentration (U_{osm}) always higher, on the constricted than on the control side. During hypotonic saline diuresis, two striking changes were seen: first, U_{Na} on the control side rose sharply, but little or no change was noted on the constricted side; second, U_{osm} on the constricted side, which was above the control side during water diuresis, fell to a value below that of the control side.

A typical experiment during acute hydronephrosis is shown in Figure 2. The results of this study disclose a pattern similar to that of renal arterial constriction. During water diuresis GFR, urinary flow, and U_{Na} were lower, whereas U_{osm} was higher, on the hydronephrotic than on the control

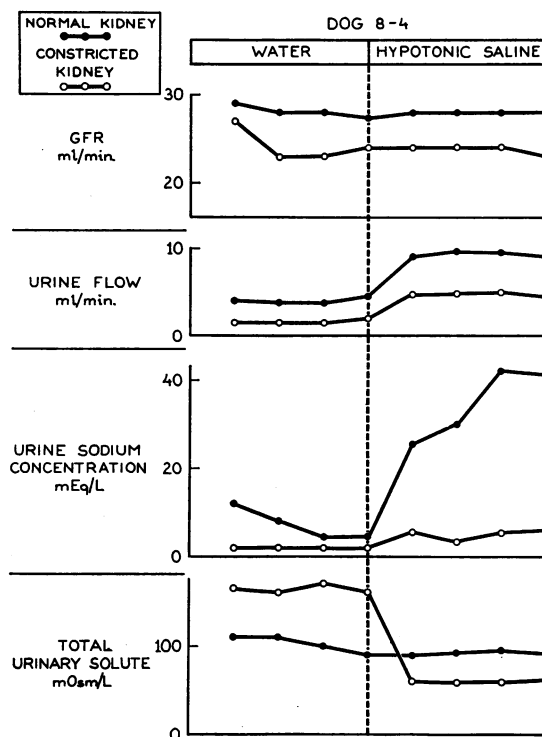


FIG. 1. THE EFFECTS OF RENAL ARTERIAL CONSTRICTION ON WATER AND ELECTROLYTE EXCRETION DURING WATER AND HYPOTONIC SALINE DIURESIS. GFR = glomerular filtration rate.

side. During hypotonic saline diuresis U_{Na} on the normal side rose with little or no change on the hydronephrotic side, and U_{osm} fell from a value above that of the normal side during water diuresis to below the normal side during hypotonic saline diuresis.

A representative experiment on an animal with chronic hydronephrosis is shown in Figure 3. In contrast to acute hydronephrosis, U_{Na} was markedly higher on the hydronephrotic than the control side during both water and hypotonic saline diuresis. The failure of the U_{osm} on the hydronephrotic side to fall from a value above that of the control side during water diuresis to below the control side during hypotonic saline diuresis also is in marked contrast to the pattern seen in both renal arterial constriction and acute hydronephrosis.

The effects of all three experimental models on the process of urinary dilution are shown in Figure 4 and the results expressed as the ratio of the experimental to the control side. Renal arterial

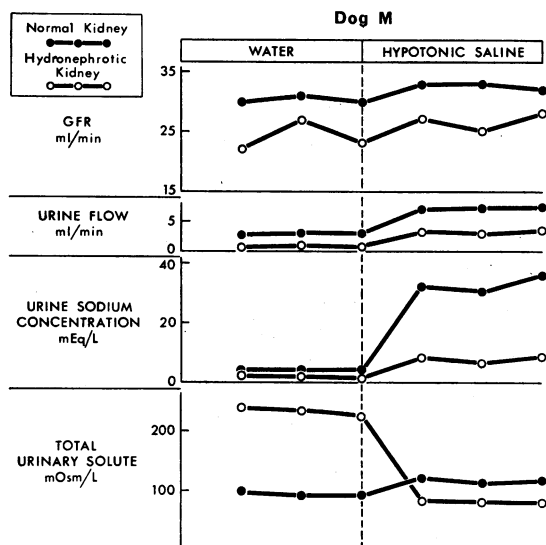


FIG. 2. THE EFFECTS OF ACUTE HYDRONEPHROSIS ON WATER AND ELECTROLYTE EXCRETION DURING WATER AND HYPOTONIC SALINE DIURESIS.

constriction and acute hydronephrosis yielded similar results: the U_{osm} from the experimental side was invariably higher during water diuresis and lower during hypotonic saline diuresis than that of the control side. In contrast, during chronic hydronephrosis U_{osm} was higher on the hydronephrotic side in both water diuresis (6 of 11 studies) and hypotonic saline diuresis (9 of 11 studies). The difference in U_{osm} between acute and chronic hydronephrosis during hypotonic saline

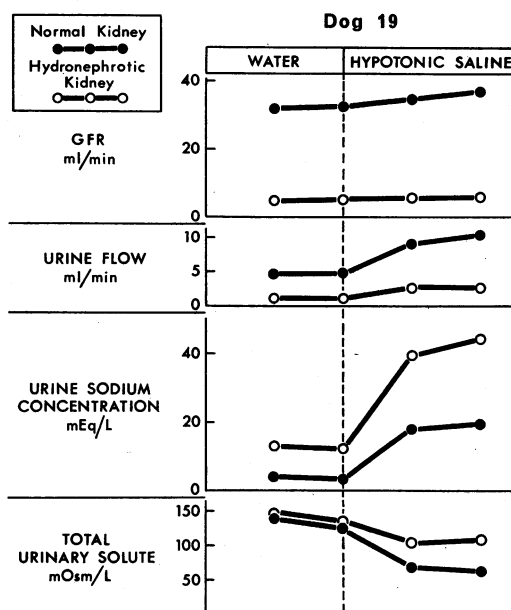


FIG. 3. THE EFFECTS OF CHRONIC HYDRONEPHROSIS ON WATER AND ELECTROLYTE EXCRETION DURING WATER AND HYPOTONIC SALINE DIURESIS. This experiment was performed 5 weeks after permanent ureteral constriction.

diuresis was highly significant with a p value of < 0.005 .¹ The effects of renal arterial constriction and acute hydronephrosis on free water clearance (C_{H_2O}) were also similar. During both water and hypotonic saline diuresis the absolute C_{H_2O}

¹ Henceforth, the p values reported refer to the difference between acute and chronic hydronephrosis.

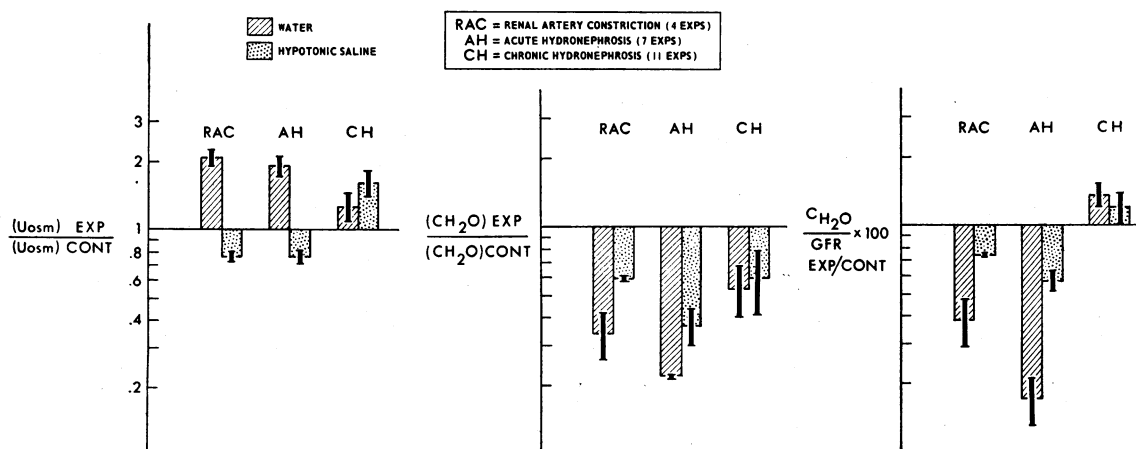


FIG. 4. THE EFFECTS OF RENAL ARTERIAL CONSTRICTION AND ACUTE AND CHRONIC HYDRONEPHROSIS ON URINARY SOLUTE CONCENTRATION (U_{osm}), ABSOLUTE SOLUTE-FREE WATER CLEARANCE (C_{H_2O}), AND FRACTIONAL FREE WATER CLEARANCE ($C_{H_2O} \times 100 / GFR$). The vertical bars represent the mean of the ratios of the experimental to the control side \pm standard error.

(Figure 4, middle panel) and the fractional excretion of free water [C_{H_2O} per 100 ml GFR (Figure 4, panel on the right)] were always lower on the side with renal arterial constriction or acute hydronephrosis than on the control side. In chronic hydronephrosis, by contrast, although the absolute C_{H_2O} was lower on the experimental than on the control side (Figure 4, middle panel), C_{H_2O} per 100 ml GFR was greater on the hydronephrotic than on the control side (Figure 4, panel on the right) in 8 of 10 studies during water diuresis ($p < 0.01$) and 7 of 10 studies during hypotonic saline diuresis ($p < 0.05$).

The effects of renal arterial constriction and acute and chronic hydronephrosis on urinary sodium are shown in Figure 5. Urinary sodium concentration was always lower on the side with renal arterial constriction than on the control side during both water and hypotonic saline diuresis. In acute hydronephrosis a pattern similar to that of renal arterial constriction was seen in all experiments. In contrast, in chronic hydronephrosis the urinary sodium concentration was always greater on the hydronephrotic side than on the

control side ($p < 0.05$ during water diuresis and < 0.005 during hypotonic saline diuresis).

The absolute rate of sodium excretion ($U_{Na}V$) and the fractional rate of sodium excretion [$(C_{Na}/\text{inulin clearance}) \times 100$] were always lower on the side with renal arterial constriction than on the control side (Figure 5). A similar effect on the absolute and fractional rates of sodium excretion was obtained in the experiments with acute hydronephrosis. Chronic hydronephrosis, on the other hand, resulted in higher absolute rates of sodium excretion in 9 of 10 experiments during water diuresis ($p < 0.01$) and 6 of 10 experiments during hypotonic saline diuresis ($p < 0.005$); the fractional rate of sodium excretion was uniformly greater on the side with chronic hydronephrosis than on the control side ($p < 0.01$ during water diuresis and < 0.005 during hypotonic saline diuresis).

The effect of acute and chronic hydronephrosis on the relationship between nephron perfusion and tubular mass was also examined. The GFR on the experimental, as compared with the control, side was reduced 24 to 42% in renal arterial con-

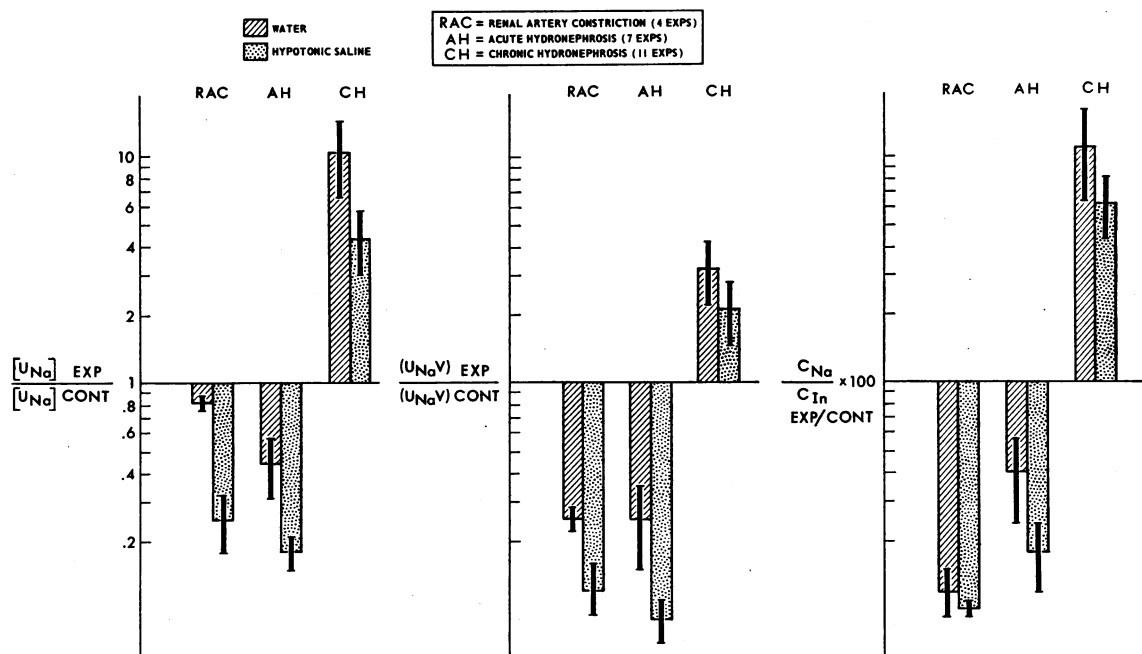


FIG. 5. THE EFFECTS OF RENAL ARTERIAL CONSTRICTION AND ACUTE AND CHRONIC HYDRONEPHROSIS ON URINARY SODIUM CONCENTRATION (U_{Na}), AND ABSOLUTE ($U_{Na}V$) AND FRACTIONAL ($C_{Na} \times 100/\text{INULIN CLEARANCE}$) RATES OF SODIUM EXCRETION. The vertical bars represent the mean of the ratios of the experimental to the control side \pm standard error.

striction, 14 to 77% in acute hydronephrosis, and 5 to 92% in chronic hydronephrosis. The Tm_{PAH} on the experimental side was reduced below that of the control side in both acute and chronic hydronephrosis. The relative effects of acute hydronephrosis and of chronic hydronephrosis on the GFR and Tm_{PAH} expressed as a ratio are shown in Table I. It is apparent that in acute hydronephrosis the ratio of the GFR to Tm_{PAH} was consistently reduced on the hydronephrotic side as compared to the control side; the ratio on the experimental side was 9 to 37% lower than on the control side, indicating that there was a disproportionate fall of GFR compared to Tm_{PAH} . These findings in acute hydronephrosis are similar to those of Thompson, Barrett, and Pitts in animals where renal underperfusion was induced by the inflation of a balloon in the aorta (13). In chronic hydronephrosis a different pattern was evident; the ratio of GFR to Tm_{PAH} was 18 to 76% higher on the hydronephrotic side than on the control side.

Discussion

The terms nephron overperfusion and nephron underperfusion are usually taken to mean increased or decreased GFR per nephron. For purposes of the present study, however, where the diluting capacity of the kidney is used as an index of perfusion, it is more useful to redefine these terms in a more restrictive sense as the amount of fluid delivered to the diluting segment, without specifying the mechanism that might be responsible for alterations in delivery rate. This requires that a standard be available in terms of which delivery rate to the diluting segment can be assessed; the contralateral control kidney serves this purpose. Thus redefined, underperfusion and overperfusion mean, respectively, reduced or increased tubular flow through individual distal nephrons,² as compared to the flow of the contralateral control kidney.

² For purposes of this discussion the distal nephron is defined as that portion of the nephron that is impermeable to water during maximal suppression of antidiuretic hormone (ADH). This presumably includes the ascending limb of Henle's loop, the distal convoluted tubule, and the collecting duct. The proximal nephron includes those segments proximal to the water-impermeable segment and consists of the proximal convoluted tubule, pars recta, and the descending limb of Henle's loop.

Constriction of the renal artery in the present experiments reduced the glomerular filtration rate by 24 to 42%. Although it has been demonstrated that glomerulotubular balance is maintained under such circumstances so that the percentage of filtrate reabsorbed in the proximal tubule remains constant (14-16), the absolute delivery of filtrate to the distal nephron is sharply reduced. Constriction of the renal artery, therefore, furnishes an excellent model to examine the pattern of urinary formation during underperfusion of the distal nephron.

Two consequences result from diminished delivery of filtrate to the distal nephron. First, sodium reabsorption is more complete and therefore the formation of solute-free water per unit volume of tubular fluid is enhanced. Second, back-diffusion of free water in the collecting duct per unit volume of tubular fluid is augmented, thereby increasing free water loss. Which of these processes will predominate during slowed flow depends principally on whether sodium reabsorption in the diluting segment is already functioning near its limiting concentration gradient. During water diuresis the concentration gradient of sodium across the distal nephron is near a maximal value. Slowed flow will augment sodium reabsorption slightly; this will increase free water formation per unit volume only minimally, but will markedly lower U_{Na} . The absolute volume of free water formed is diminished due to the reduction of the volume of fluid delivered to the diluting segment. An additional effect of slowed flow during water diuresis will be seen in the collecting duct where the loss of the same, or even reduced, absolute amounts of free water from a markedly diminished volume of fluid will result in a sharp reduction in C_{H_2O} per unit volume of tubular fluid and a rise in U_{osm} .

During water diuresis, therefore, the side with renal arterial constriction will display a reduced rate of C_{H_2O} because reduced delivery of filtrate to the diluting segment diminishes free water formation; a lower U_{Na} because the magnitude of reabsorption during slowed flow, though small in absolute amount, is proportionately greater than the rate of back-diffusion of free water; and a higher U_{osm} because free water back-diffusion concentrates nonsodium solutes, principally urea.

even though the excretion of urea is sharply reduced owing to a fall in GFR.

During hypotonic saline diuresis without renal arterial constriction (Figure 1, normal kidney) expansion of extracellular fluid volume results in increased delivery of tubular fluid to the distal nephron; this is associated with a greater production of free water and rise in U_{Na} with little change in U_{osm} . The constancy of U_{osm} while U_{Na} rises sharply is a result of the dilution of nonsodium urinary solutes by the increased excretion of sodium-containing urine.

During hypotonic saline diuresis the superimposition of renal arterial constriction results in a fall in the urinary concentrations of both sodium and total solute (Figure 1, panel on right). The reduced U_{osm} is the opposite effect from that observed when the renal artery is constricted during water diuresis. Since, under the condition of increased sodium delivery (hypotonic saline diuresis), the diluting segment is operating above its limiting concentration gradient, the greatly increased reabsorption of sodium as a result of slowed flow (renal arterial constriction) will augment the formation of solute-free water per unit tubular volume. In consequence, U_{Na} and U_{osm} fall. The fall in U_{osm} on the constricted side during the transition from water diuresis to hypotonic saline diuresis (Figure 1) is attributable to dilu-

tion of nonsodium urinary solutes by augmented urinary flow.

These findings define the physiologic pattern of distal nephron underperfusion. During water diuresis acute reduction in GFR results in decreased U_{Na} (Figure 5) and increased U_{osm} (Figure 4), whereas in hypotonic saline diuresis reduced GFR diminishes both U_{Na} and U_{osm} ; C_{H_2O} per 100 ml GFR is reduced during water diuresis and hypotonic saline diuresis (Figure 4). Since the findings in acute hydronephrosis are similar to those in renal arterial constriction, we conclude that acute hydronephrosis produces underperfusion of the distal nephron.

The pattern of renal function observed in chronic hydronephrosis differed markedly from that resulting from renal arterial constriction and acute hydronephrosis. The chronically hydronephrotic kidney compared with its contralateral control displayed a higher U_{Na} , a higher absolute and fractional $U_{Na}V$ (Figure 5), a higher U_{osm} during water diuresis that did not fall during hypotonic saline diuresis (Figure 4), and a lower C_{H_2O} (Figure 4).

This pattern of renal function in chronic hydronephrosis could represent the superimposition of tubular damage on the distal underperfusion characteristic of acute hydronephrosis. Tubular damage, by impairing sodium transport in the diluting

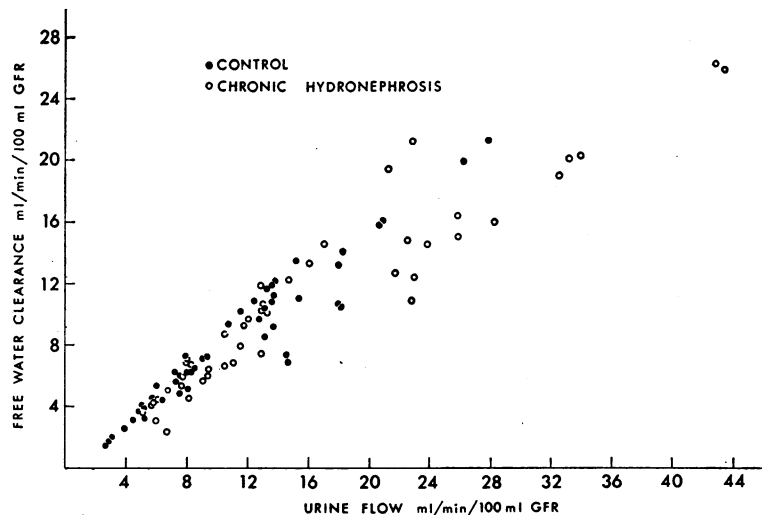


FIG. 6. FRACTIONAL FREE WATER CLEARANCE AT VARYING FRACTIONAL RATES OF URINARY FLOW IN CHRONIC HYDRONEPHROSIS AS COMPARED TO NORMAL. Points represent values obtained during both water and hypotonic saline diuresis.

TABLE I

The ratio of glomerular filtration rate (GFR) to maximal tubular transport rate for p-aminohippurate (T_{PAH}) in acute and chronic hydronephrosis

Experimental model	GFR/ T_{PAH}		
	Experimental	Control	Exp./Cont.
Acute hydronephrosis	6.3	8.3	0.8
	4.8	7.7	0.6
	7.1	9.9	0.7
	9.5	10.5	0.9
Mean \pm SD	6.9 \pm 1.7	9.1 \pm 1.1	0.75* \pm 0.1
Chronic hydronephrosis	10.7	8.3	1.3
	12.5	7.1	1.8
	13.0	8.8	1.5
	5.4	4.6	1.2
Mean \pm SD	10.4 \pm 3.0	7.2 \pm 1.6	1.45* \pm 0.2

* $p < 0.01$.

segment, could result in the high U_{Na} , high U_{osm} , and low $C_{\text{H}_2\text{O}}$ characteristic of chronic hydronephrosis.

To examine the functional integrity of the diluting segment, we plotted $C_{\text{H}_2\text{O}}$ per 100 ml GFR against urinary flow (V) per 100 ml GFR (Figure 6). $C_{\text{H}_2\text{O}}$ was plotted against V rather than solute clearance (C_{osm}) because the rate of urinary flow in water diuresis is a closer approximation of the rate of delivery of filtrate to the loop of Henle than is C_{osm} .³ If free water formation were significantly impaired, less $C_{\text{H}_2\text{O}}$ should be found on the hydronephrotic than on the normal side at any given rate of urinary flow. This is, however, not the case. It is apparent from Figure 6 that, at comparable rates of delivery, the normal and chronically hydronephrotic kidneys generate the same $C_{\text{H}_2\text{O}}$. Therefore, there is no apparent defect in $C_{\text{H}_2\text{O}}$ in chronic hydronephrosis.

Since $C_{\text{H}_2\text{O}}$ represents a balance between free water formation and free water back-diffusion, it might be argued that a defect in formation could be masked by a commensurate reduction in back-diffusion. The shrinkage and scarring of the medulla so characteristic of chronic hydronephrosis undoubtedly prevents the establishment of

³ During water diuresis the distal convoluted tubule and the collecting duct are relatively impermeable to water. The rate of urinary flow, therefore, is the best index of the rate of delivery of tubular fluid to the distal nephron. Urinary flow, however, does not equal the rate of delivery since some back-diffusion of water from the collecting duct is known to occur even in the absence of ADH (8, 11, 17, 18).

medullary hypertonicity and impairs diffusion of water out of the collecting duct. However, reduction in free water loss would contribute equally to urinary flow and $C_{\text{H}_2\text{O}}$. Consequently, although a reduction in free water back-diffusion would increase $C_{\text{H}_2\text{O}}$, it would not correct the low $C_{\text{H}_2\text{O}}$ to a normal value when $C_{\text{H}_2\text{O}}$ is compared to urinary flow. Since the relations between $C_{\text{H}_2\text{O}}$ and urinary flow in the normal and hydronephrotic kidney are superimposable, this would constitute evidence against the hypothesis that the pattern of urinary formation in chronic hydronephrosis is attributable to a combination of underperfusion of nephrons, tubular damage, and reduced free water back-diffusion. None of these arguments excludes the possibility that some degree of tubular damage might exist, and that free water back-diffusion might be reduced. Indeed, the profound destruction of the medulla almost certainly means that the normal back-diffusion of free water is drastically curtailed. We merely wish to emphasize that the combination of tubular damage and reduced free water back-diffusion cannot readily explain the striking increase in sodium excretion in the face of normal $C_{\text{H}_2\text{O}}$ in the setting of distal nephron underperfusion.

The changes in sodium and water excretion in chronic hydronephrosis can be more easily explained on the basis of reduced nephron mass with overperfusion of residual nephrons. It is not unreasonable to assume that the GFR per nephron in chronic hydronephrosis is elevated. Although intrapelvic pressure rises sharply with acute obstruction of the ureter, it has been shown that with the persistence of obstruction the intrapelvic pressure falls gradually towards normal values (9). Despite the fall in intrapelvic pressure some nephrons never regain function and the functional renal mass is reduced. When the intrapelvic pressure falls, however, the remaining nephrons of the hydronephrotic kidney may respond in a similar manner to those of a kidney damaged from any other cause by a compensatory increase in the rate of filtration per nephron (19).

Furthermore, the data relating the GFR to renal tubular mass (T_{PAH}) are consistent with the presence of increased GFR per nephron in chronic, as distinct from acute, hydronephrosis (Table I). In renal underperfusion due to inflation of a balloon in the aorta a fall in maximal tubular trans-

port of glucose (Tm_{glucose}) (13) has been reported. Acute elevation of ureteral pressure has also been reported to result in a reduction in Tm_{glucose} (10) and Tm_{PAH} [(10) and present study]. In both experimental procedures the fall in GFR almost always exceeded the fall in the tubular maximum, thus suggesting a reduced filtration rate per nephron. In chronic hydronephrosis, however, the fall of Tm_{PAH} was always in excess of the fall in GFR. The increased GFR per Tm_{PAH} may be interpreted as an increased filtration rate per nephron.

It is likely, therefore, that the combination of an elevated GFR per nephron and diminished fractional reabsorption of filtrate in the proximal nephron results in marked overperfusion of the distal nephron. The larger volume of fluid delivered to each distal nephron results not only in greater $C_{\text{H}_2\text{O}}$ per 100 ml GFR, but also in a higher rate of sodium excretion and a higher U_{osm} in water diuresis. The low absolute rates of $C_{\text{H}_2\text{O}}$ must be due to a diminution in the total number of nephrons.

The striking difference in the pattern of water excretion between acute and chronic hydronephro-

sis is displayed in Figure 7, where the fraction of the glomerular filtrate excreted into the urine (V/GFR) on the experimental side is compared to that of the contralateral control kidney during both water and hypotonic saline diuresis. It is evident that at any given level of fractional volume excretion on the control side, fractional excretion is lower on the side with renal arterial constriction or acute hydronephrosis and higher on the side with chronic hydronephrosis. The proportion of the GFR that is excreted into the urine during maximal suppression of antidiuretic hormone represents the difference between fractional delivery to, and fractional water loss from, the distal nephron. The low fractional volume excretion during acute hydronephrosis and renal arterial constriction is probably the consequence of diminished delivery of filtrate to the diluting segment in the face of a well-maintained absolute rate of free water back-diffusion out of the collecting duct. The well-maintained absolute rate of free water back-diffusion will result in an increased fractional loss of water and a diminished fractional volume excretion. The demonstration by Levinsky, Davidson, and Berliner (20) that during antidiuresis

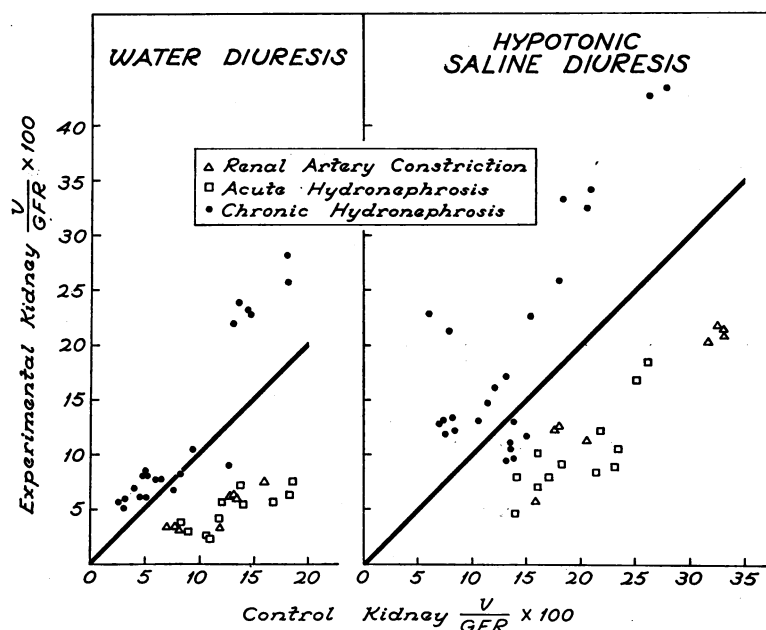


FIG. 7. FRACTION OF GFR ($V/\text{GFR} \times 100$) DELIVERED TO THE DILUTING SEGMENT IN RENAL ARTERIAL CONSTRICTION AND ACUTE AND CHRONIC HYDRONEPHROSIS, COMPARED TO THE CONTROL SIDE. Graph to the left represents data obtained during water diuresis, graph to the right during hypotonic saline diuresis. Lines drawn are the theoretic lines of equal fractional delivery.

renal arterial constriction sufficient to reduce GFR by 50% results in only a 15 to 20% reduction in medullary sodium concentration supports the view that medullary hypertonicity is preserved despite underperfusion of the distal nephron.

The increased fractional volume excretion during chronic hydronephrosis could result from two factors. Unquestionably the diminution in free water back-diffusion secondary to medullary destruction contributes to the augmented fractional volume excretion. A second contributing factor, also the consequence of medullary destruction, would be diminished loss of fluid from the descending limb of Henle's loop (21) resulting in increased fractional delivery of filtrate to the diluting segment.

Clinically, chronic hydronephrosis is characterized by a marked propensity towards polyuria with impaired concentrating ability, which at times reaches the proportions of frank nephrogenic diabetes insipidus (1-5). This syndrome occurs with some frequency in hypocalcemic and hypokalemic nephropathy, but only rarely in parenchymal renal disease (1, 22-24). Since most forms of chronic renal insufficiency do not produce nephrogenic diabetes insipidus, there must be something distinctive in chronic hydronephrosis that predisposes to this derangement. A plausible explanation may reside in the gross anatomical differences between chronic hydronephrosis and other forms of renal disease. The renal parenchyma in hydronephrosis of some duration is thinned out with flattening of the papilla and narrowing of the medulla, whereas in other forms of renal disease, medullary renal architecture is better preserved. The disproportionately severe destruction of the medulla in chronic hydronephrosis results in diminished medullary tonicity, which may increase the excretion of dilute urine by two derangements. First, the abstraction of water from the descending limb of Henle's loop will be greatly reduced; the resulting augmentation of fractional delivery of filtrate to the diluting segment will increase free water formation. Second, free water back-diffusion out of the collecting duct will be greatly reduced. The combination of increased free water formation and reduced free water loss could account for the increased frequency of nephrogenic diabetes insipidus in chronic hydro-

nephrosis, as contrasted to other forms of parenchymal renal disease.

Summary

The effects of acute and chronic hydronephrosis on renal function were investigated and compared to those of renal arterial constriction during water and hypotonic saline diuresis.

In acute hydronephrosis there was a reduction in urinary sodium concentration, sodium excretion, and free water clearance (C_{H_2O}) per 100 ml glomerular filtration rate (GFR). The urinary osmolality was higher on the hydronephrotic side than on the control side during water diuresis and fell to below that of the control side during hypotonic saline diuresis. This pattern was similar to that of renal arterial constriction and, therefore, was due to distal nephron underperfusion.

Chronic hydronephrosis resulted in a markedly different pattern characterized by an increase in urinary solute concentration, urinary sodium concentration, and sodium excretion; C_{H_2O} was decreased, whereas C_{H_2O} per 100 ml GFR was increased. This pattern is best explained by a combination of reduced renal mass with overperfusion of residual nephrons as a result of increased filtration and diminished fractional reabsorption in the proximal nephron. Reduced back-diffusion of free water in the distal nephron may also contribute to the increased fractional excretion of water.

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