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# Renal Function in Chronic Hydronephrosis with and without Infection and the Role of the Lymphatics. An Experimental Study in Dogs

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Summary. Renal function, rate of urine turnover in the renal pelvis, and the role of the renal lymphatics were studied in dogs during total ureteral occlusion lasting from 6 to 34 days with and without induced infection. - Glomerular filtration rate, effective renal plasma flow, concentration ability, and tubular reabsorption of sodium and potassium were followed. The concentrations of 2 radiolabelled clearance substances, iothalamate and o-iodohippurate, as well as those of sodium, potassium, and total protein were determined in hilar and/or subcapsular lymph obtained by cannulization of the lymphatics. - In uninfected hydronephrosis, concentration ability as well as sodium and potassium reabsorption were impaired as compared with control kidneys. In infected hydronephrosis, these partial functions were not maintained. Turnover in the occluded renal pelvis, ranged from 0.04 to 0.16 ml per minute. Following ureteral occlusion of 1 week, pyelolymphatic reabsorption into hilar, but not subcapsular lymph could be demonstrated.

Key words: Renal function, chronic hydronephrosis, renal lymphatics

Following relief of chronic ureteral obstruction the kidney has an excellent recuperative faculty. It has been established that this process is stimulated by contralateral nephrectomy. If the obstruction is present for a certain length of time, abnormalities in salt and water excretion will occur at least temporarily following ureteral release (2). If obstruction is combined with infection, destruction of the kidney is rapid (11). It has also been demonstrated that once an obstructed kidney is infected, it is extremely difficult if not impossible to eradicate the infection as long as the obstruction remains (10, 25).

Experimental investigations of chronically obstructed kidneys with and without infection concerning renal lymph and turnover rate in the renal pelvis are of great clinical importance for therapeutic and diagnostic reasons: In order to treat infected kidneys effectively, antibacterial agents must reach sufficient concentrations in the renal interstitium and urine. No studies, however, are available concerning lymph formation in chronic hydronephrosis. Such studies may give information on the interstitial space. The concentration of substances administered for therapeutic or diagnostic reasons, e. g. antibacterial agents and contrast media, which can be obtained in the occluded renal pelvis depends on the duration of effective plasma concentration, renal excretion and rate of turnover in the occluded pelvis.

Since a method of determining the rate of turnover in the renal pelvis and renal function following total ureteral occlusion had been developed (15), we applied this method in combination with lymph studies in order to investigate these questions.

## Material and Methods

The study was performed in 13 mongrel dogs (weight from 12 to 30 kg). The dogs were an-

esthesized with thiopental sodium (30 mg per kg of body weight) intravenously. Subsequently, additional thiopental sodium was administered to maintain constant relaxation. Through a small incision through the left lower abdomen the left ureter was transected prevesically. Following this procedure the dogs were divided into three groups: The first group (4 dogs: No. 50, 51, 52, 58) remained uninfected and was further investigated after 6 to 8 days. The second group (3 dogs: No. 59, 60, 63) remained uninfected and was investigated after 29 to 34 days. The third group (6 dogs) was infected the day after ureteral occlusion by intravenous injection of approximately $4 \times 10^9$ E. coli (serotyped as 06). Two dogs died the following day, probably of septicemia. The remaining 4 dogs (No. 53, 54, 55, 56) were investigated 6 to 11 days following the introduction of infection. The experimental procedure was performed in the 3 groups according to a previously developed technique (15).

Under anesthesia, polyethylene cannulas were inserted into the aorta and vena cava through a femoral cutdown. Arterial pressure was continuously recorded via a Statham pressure transducer on a Gilson recorder. For better visualization of the renal lymphatics, 2 ml of Direct Sky Blue$^R$ 4% (Wyeth Lab.) was administered intravenously together with a prime dose of 0.5 µ Ci per kg of $^{125}$I-iothalamate (Glofil$^R$, Abbott Laboratories) and $^{131}$I-o-iodohippurate (Hippuran$^R$, Abbott Laboratories). Following this, constant intravenous infusions of 5% glucose and 0.9% NaCl were administered throughout the experiment, at a rate of 4 ml per minute of each fluid. The 2 radiolabelled substances were added to the 0.9% NaCl solution (100 µ Ci per 1000 ml).

The right ureter was cannulated through a small right lower abdominal incision. For continuous urine drainage the left kidney was exposed through a flank incision and the left renal pelvis was cannulated through a ureteral incision distal to the ureteropelvic junction, but urine was not allowed to drain from the left renal pelvis. A hilar and/or subcapsular lymph vessel was cannulated with a 26 gauge needle connected to a silastic tubing (Dow Corning, 0.012" i.d., 0.025" o.d.).

After sufficient equilibration time (at least 90 min), urine was collected from the right kidney (control kidney) in 30 minute clearance periods for 150 to 300 min. Arterial blood samples were taken at the midpoint of each clearance period. From the left renal pelvis 1.0 ml of urine was removed and reinjected after adding a known amount (4 to 12 µ Ci) of $^{99m}$Tc pertechnetate (Mallinckrodt). In one experiment (No. 56) $^{99m}$Tc-diethylenetriaminepentaacetic acid (DTPA) (Renotec$^R$, Squibb) was used instead. The content of the renal pelvis was mixed 3 to 5 times by removing and immediately gently reinjecting a fluid amount of approximately 3 to 5 ml. Following this 0.3 to 0.5 ml of urine was removed for analysis and calculation of distribution space. Further urine specimens were taken at intervals of 30 to 60 min. At the end of the experiment all urine was aspirated from the renal pelvis within a few seconds and in several portions. In group 2 one dog (No. 59) had to be excluded from further evaluation because of hypotensive shock during the operation, as indicated by arterial pressure recording and lack of urine output from the right (control) kidney. No absorption from the occluded renal pelvis could be demonstrated within 2 h. In another experiment (No. 60) of this group the concentration decrease of $^{99m}$Tc pertechnetate in the renal pelvis was found to be only around 10% within 3 1/2 h, and the procedure was therefore modified in the third dog (No. 63): 22 h prior to the actual experiment 200 µ Ci of $^{99m}$Tc-pertechnetate were injected into the renal pelvis through a small flank incision as described above. The concentration of pertechnetate in the renal pelvis in this dog decreased to 40% the following day, thus improving the calculation of the turnover rate.

The radiolabelled substances were counted in an automatic gamma scintillation counter (Packard) at proper window settings. $^{99m}$Tc was counted on the day of the experiment, $^{125}$I and $^{131}$I two to three days later in order to allow $^{99m}$Tc to decay (half life 6 h). All counts were corrected for overlap. Sodium and potassium were analyzed in a Beckman flame photometer, total protein according to the biuret method (26).

Calculation of the volume of the renal pelvis was performed in 2 ways: by calculating the distribution space of injected $^{99m}$Tc pertechnetate and by measuring the urine volume at the end of the experiment by aspiration in portions. The rate of turnover and amount of absorbed urine volume from the renal pelvis per unit of time was calculated from the volume of the renal pelvis and the concentration decrease of $^{99m}$Tc pertechnetate following injection into the renal pelvis. Theory and details of these calculations are described elsewhere (15). The actual urine concentration of the 2 clearance substances, iothalamate and o-iodohippurate, i.e. the concentration of urine entering the renal pelvis from the collecting ducts, was calculated from the data of the urine portions aspirated at the end of the experiment. In these urine portions a concentration increase of iothalamate and o-iodohippurate and a concentration decrease of $^{99m}$Tc pertechnetate was measured. This can only be due to additional urine having entered from the collecting ducts after pressure release, since reabsorption from the renal pelvis and new renal urine production must be considered insignificant within that short period of time. Recirculation of absorbed $^{99m}$Tc pertechnetate is also negligible (16). The clearance of iothalamate, considered as glomerular filtration rate (GFR) (20), and that of o-ioduhippurate, considered as effective renal plasma flow (ERPF), were calculated according to the usual clearance formula $(U \times V) / P$, using the

amount of reabsorbed urine from the renal pelvis as "urine flow" (V), the calculated actual urine concentration (U) and the plasma concentration (P) of the corresponding clearance substance.

## Results

Bacteriological examination of urine specimens at the beginning of the experiment showed that urine of all control kidneys and uninfected hydronephrotic kidneys was sterile. All urine samples of infected hydronephrotic kidneys were purulent with colony counts of more than $10^6$ per ml.

Hilar, and in particular, subcapsular lymph vessels were prominent in all uninfected kidneys occluded for one week. If no data are listed cannulation was not possible for technical reasons although lymph vessels could be seen. In the kidneys occluded for 34 days, subcapsular lymph vessels were distended, but lymph flow was significantly reduced. In one dog (No. 60) only tiny hilar lymph vessels could be seen.

In group 3 (infected kidneys) only in one kidney (No. 56) was it technically possible to cannulate a subcapsular lymph vessel, but no hilar one. In the other dogs of this group only very tiny subcapsular lymph vessels could be seen. The renal capsule was inflamed and thickened.

In Table 1 the subcapsular and in Table 2 the hilar lymph concentrations are listed as ratios to the corresponding arterial plasma concentrations.

Iothalamate concentration ratios between subcapsular lymph and arterial plasma were slightly, but significantly lower than unity in the 2 kidneys occluded for 34 days. In hilar lymph no statistically significant difference from arterial plasma concentration could be detected.

O-iodohippurate concentration ratios between subcapsular lymph and arterial plasma, however, were found to be significantly lower than unity in all 3 groups, whereas in hilar lymph only in 1 dog (group 2) the ratio was less than unity.

Sodium and potassium in hilar as well as in subcapsular lymph were found to be statistically no different from the arterial plasma concentrations in all three groups. The total protein concentration ranged between 14 and 37% of the plasma concentration in group 1 and 2, whereas in the infected kidneys a higher protein content was found (54 to 74%).

When the lymph concentrations of the various substances were compared to each other, only the subcapsular lymph concentration ratios between o-iodohippurate and iothalamate in group 1 was below unity. This ratio is similar to that in freely draining kidneys (15). In the other group, and in hilar lymph, there is no or only a slight difference between the two clearance substances.

Results obtained from injection of the test substances, $^{99m}$Tc pertechnetate and $^{99m}$Tc DTPA respectively, into the renal pelvis are listed in Table 3. The total volume of the renal pelvis was considerably larger in group 2 than in group 1 and 3. The rate of turnover was correspondingly variable. The calculated "urine flow", however, was fairly equal in all three groups (0.04 to 0.16 ml per min) except experiment No. 52. In this experiment an artificial rupture of the pelvic lining may have occurred following injection of the test substance.

The lymph concentrations of the test substances in hilar lymph were less than 1% of the urine concentrations and in subcapsular lymph even less than 0.05%.

Only in group 1 a urine concentration of iothalamate exceeding the arterial plasma concentration could be reached in the occluded renal pelvis during the priod of constant infusion (3 to 4 h). The calculated actual urine concentration, however, was still not reached within that period of time (Table 4). In the infected hydronephrotic kidneys there was no indication that concentration ability was maintained since the calculated urine concentration ratios of iothalamate were close to unity.

The clearance of o-iodohippurate (ERPF) exceeded the clearance of iothalamate (GFR) in all 3 groups, indicating active tubular secretion. The excretion fraction of the filtered sodium indicated that tubular sodium reabsorption was still high in group 1, reduced in group 2, and absent in group 3. In 2 control kidneys of group 3 a reduced sodium and absent potassium reabsorption could be demonstrated (No. 54, 55). In these 2 dogs the GFR of the control kidneys was also reduced, indicating renal impairment probably caused by the intravenous injection of E. coli, although urine from the control kidneys was found to be sterile. Potassium reabsorption in the occluded kidney was also reduced as compared with the control kidney.

## Discussion

Hydronephrosis is the result of imbalance between urine formation, excretion or reabsorption. The kidney reacts to obstruction first by evidence of trauma, then by compensatory backflow with progressive dilation in which the rate of excretion is slightly greater than that of reabsorption and, finally, by atrophy as the secretory ability of the parenchyma is destroyed (9).

Numerous experimental studies have shown that after 2 to 6 weeks of ureteral obstruction atrophy of renal parenchyma becomes irreversible. Following ureteral occlusion over 40 days renal function decreases to only 10% (13). Although in our experiments there is no significant difference concerning the length of occlusion in groups 1 and 3, more severe renal damage can be expected in group 3 because of infection. Group 2 may be considered as somewhere in between the 2 other groups.

### Change in Renal Function

Using for the first time standard renal clearance tests, Kerr (13) studied the effect of complete ureteral obstruction for 1 to 4 weeks, as we did in our model. Despite no marked effect on the micros-

Table 1. Composition of renal subcapsular lymph during chronic hydronephrosis (mean ± SE)

| Dog No. | | Length of occlusion (days) | Periods (No.) | Flow µl/min | Subcapsular lymph / arterial plasma ratio: Iothalamate (I) | Hippurate (H) | Sodium (Na) | Potassium (K) | Protein (Pt) | Relative lymph ratios H/I | I/Na | K/Na |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 50 | Non-infected | 6 | 8 | 189±42 | 1.05±0.06 | 0.85±0.04 | 0.94±0.03 | 1.14±0.07 | 0.14±0.03 | 0.81±0.05 | 0.89±0.05 | 1.22±0.07 |
| 51 | | 6 | 7 | 84±21 | 0.90±0.04 | 0.58±0.07 | 0.99±0.06 | 1.02±0.06 | 0.37±0.16 | 0.65±0.07 | 0.92±0.08 | 1.04±0.06 |
| 52 | | 7 | 5 | 66±18 | 1.02±0.03 | 0.71±0.03 | 0.96±0.05 | 0.95±0.05 | 0.20±0.09 | 0.74±0.02 | 1.01±0.05 | 0.99±0.04 |
| 60 | | 34 | 5 | 29±18 | 0.86±0.09 | 0.83±0.07 | - | - | - | 0.97±0.12 | - | - |
| 63 | Inf. | 34 | 4 | 6± 2 | 0.90±0.07 | 0.90±0.05 | 1.07±0.01 | 1.05±0.33 | 0.26 (1) | 1.00±0.08 | 0.87±0.02 | 0.88±0.27 |
| 56 | | 12 | 8 | 50± 8 | 1.01±0.02 | 0.93±0.03 | 0.96±0.04 | 0.96±0.04 | 0.54 (1) | 0.93±0.04 | 1.05±0.05 | 1.00±0.03 |

(n) no. of observations if different from no. of collecting periods

Table 2. Composition of renal hilar lymph during chronic hydronephrosis (mean ± SE)

| Dog No. | | Length of occlusion (days) | Periods (No.) | Flow µl/min | Hilar lymph / arterial plasma ratio: Iothalamate (I) | Hippurate (H) | Sodium (Na) | Potassium (K) | Protein (Pt) | Relative lymph ratios H/I | I/Na | K/Na |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 51 | Non-infected | 6 | 7 | 78±25 | 1.10±0.21 | 1.15±0.07 | 0.98±0.05 | 1.21±0.33 | 0.31±0.17 | 1.15±0.53 | 1.27±0.42 | 1.23±0.30 |
| 52 | | 7 | 5 | 33± 9 | 0.98±0.04 | 1.08±0.29 | 1.01±0.05 | 1.29±0.22 | 0.27±0.05 | 1.10±0.30 | 0.97±0.07 | 1.27±0.16 |
| 63 | | 34 | 7 | 14± 4 | 0.98±0.07 | 0.90±0.03 | 1.13±0.14 | 0.94±0.15 | 0.19 (2) | 0.92±0.05 | 0.86±0.12 | 0.83±0.18 |
| 53 | | 8 | 6 | 82±23 | 1.05±0.04 | 0.96±0.03 | 1.02±0.08 | 1.09±0.08 | 0.56±0.28 | 0.92±0.04 | 1.04±0.12 | 1.07±0.05 |
| 54 | Infect. | 8 | 8 | 43±21 | 1.01±0.02 | 1.07±0.04 | 1.11±0.26 | 1.12±0.26 | 0.74±0.13 | 1.07±0.05 | 0.93±0.17 | 1.01±0.09 |
| 55 | | 7 | 5 | 35± 3 | 0.93±0.05 | 0.91±0.04 | 1.17±0.16 | 1.12±0.16 | - | 0.99±0.44 | 0.82±0.13 | 1.43±0.28 |

(n) no. of observations if different from no. of collecting periods

Table 3. Reabsorption from the renal pelvis following chronic ureteral occlusion.

| Dog No. | | Length of occlusion (days) | Volume of renal pelvis (ml) | Rate of turnover (% Vol/min) | "Urine flow" (ml/min) | $\frac{LS_T \times 100}{U_T}$ | $\frac{LH_T \times 100}{U_T}$ |
|---|---|---|---|---|---|---|---|
| 50 | | 6 | 22 | 0.60 | 0.13 | 0.04 | - |
| 51 | | 6 | 39 | 0.14 | 0.05 | - | 0.19 |
| 52 | Non-infected | 7 | 43 | 1.26 | 0.54 | 0.05 | 0.90 |
| 58 | | 8 | 35 | 0.11 | 0.04 | - | - |
| 60 | | 34 | 100 | 0.05 | 0.05 | 0.004 | - |
| 63 | | 34 | 265 | 0.06 | 0.16 | - | - |
| 53 | | 8 | 8 | 1.00 | 0.08 | - | 0.09 |
| 54 | Infected | 8 | 7 | 1.50 | 0.11 | - | - |
| 55 | | 7 | 22 | 0.60 | 0.13 | - | - |
| 56 | | 12 | 48 | 0.13 | 0.06 | - | - |

T = test substance injected into the occluded renal pelvis ($^{99m}$Tc pertechnetate or $^{99m}$Tc DTPA), LS = subcapsular lymph concentration, LH = hilar lymph concentration, U = urine concentration

copic appearance of the kidney obstructed for 1 week, he found 1 hour after ureteral release that the GFR and ERPF of the previously obstructed kidney were 25% and 27% respectively of the preligation control value, and the GFR and ERPF of the control kidney increased to 165% and 167% respectively of the control value. Maximum recovery occurred after 4 to 57 days. The ability of the previously obstructed kidney to concentrate urine, but not to dilute urine, was impaired. Following 4 weeks of ureteral obstruction, recovery was markedly reduced. Removal of the contralateral kidney caused an elevation of plasma nonprotein nitrogen which never returned to normal. After removal of the control kidney, however, renal clearances increased, demonstrating that even such kidneys can be stimulated to increase GFR and ERPF. Similar results have been found by other authors investigating renal recovery following chronic ureteral occlusion (2, 3, 4).

In our experiments we also could show impaired concentrating ability following ureteral occlusion for 1 week. The glomerular filtrate, however, was still concentrated 5 to 10 times, as demonstrated by the urine arterial plasma ratio of iothalamate. In acute hydronephrosis the kidney is able to concentrate the filtered fluid amount by more than 100 fold (15). Even after 4 weeks of ureteral occlusion, the renal concentration mechanism has not ceased. In cases of infected hydronephrosis, however, no urine concentration ability can be detected after just 1 week of occlusion.

Investigators agree that the reduced concentrating ability in the occluded kidney is connected with the loss of osmotic gradient from cortex to medulla (2). In autoradiographic studies with $^{24}$Na (19), lowered sodium concentration could be demonstrated in the papilla of the hydronephrotic kidney. The reason for this can be seen in the lowered sodium load caused by decreased GFR (14), as well as in impaired tubular sodium reabsorption caused by altered hemodynamics. As was shown by Ullrich et al. (23), the countercurrent multiplier system depends on an intact renal circulation for its continued existence both for continued filtration through the glomeruli and also for the removal of water and solutes at the appropriate rate in the vasa recta of the medulla. Local impairment of the renal circulation might therefore impair the counter-current mechanism and the urine would be less concentrated. Sodium reabsorption is reduced after only 1 week of ureteral occlusion as compared with the control kidney and with acute hydronephrosis (15). After 34 days of occlusion 70% of the filtered sodium was still absorbed, whereas no sodium at all was absorbed in infected hydronephrosis. Tubular secretion of o-iodohippurate, however, was active even in infected kidneys. Renal cortical function therefore outlasts medullary function in infected hydronephrosis.

Table 4 a. Occluded Kidney. Renal function during chronic hydronephrosis (mean ± SE)

| Dog No. | | Length Occl. (days) | Per-iods (No.) | $U_I/P_I$ | $U_I/P_I^*$ | GFR* ml/min | ERPF ml/min | $\frac{ERPF^*}{GFR}$ | $U_{Na}/P_{Na}$ | $U_K/P_K$ | $(C_{Na}/GFR)$ x 100 | $(C_K/GFR)$ x 100 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 50 | Non-infected | 6 | 10 | 5.90±1.00 | 10.8 | 1.40 | 4.1 | 2.9 ±0.3 | 0.60±0.11 | 8.20±1.70 | 6.0 | 75.7 |
| 51 | | 6 | 9 | 1.80±1.50 | 6.4 | 0.32 | 1.0 | 3.4 ±0.3 | 0.87±0.06 | 8.10±0.60 | 13.6 | 125.0 |
| 52 | | 7 | 9 | 2.30±0.70 | 6.1 | 3.30 | 19.1 | 5.8 ±0.7 | 0.79±0.07 | 6.60±0.40 | 12.9 | 107.0 |
| 58 | | 8 | 4 | 0.90±0.10 | 5.6 | 0.22 | 1.0 | 5.1 ±0.6 | 0.80±0.04 | 3.60±0.40 | 14.0 | 64.3 |
| 60 | | 34 | 5 | 0.12±0.08 | 2.7 | 0.14 | 0.5 | 3.5 ±0.3 | - | - | - | - |
| 63 | | 34 | 7 | 0.34±0.18 | 4.0 | 0.66 | 1.9 | 2.8 ±0.3 | 1.10 | 2.00 | 30.0 | 50.0 |
| 53 | Infected | 8 | 6 | 0.16±0.03 | 1.0 | 0.08 | 0.10 | 1.2 ±0.2 | 1.06±0.14 | - | 106.0 | - |
| 54 | | 8 | 8 | 0.74±0.04 | 1.0 | 0.11 | 0.19 | 1.7 ±0.4 | 1.26±0.29 | - | 126.0 | - |
| 55 | | 7 | 8 | 0.22±0.10 | 1.0 | 0.05 | 0.16 | 3.2 ±0.9 | 0.82±0.18 | - | 82.0 | - |
| 56 | | 12 | 3 | 0.34±0.12 | 1.0 | 0.06 | 0.10 | 2.0 ±0.2 | - | - | - | - |

* calculated from "actual" urine concentration (explanation see text)

I = iothalamate, Na = sodium, K= potassium, U = urine concentration,

P = arterial plasma concentration, C = clearance, GFR = clearance of iothalamate, ERPF = clearance of o-iodohippurate.

Table 4b. Control Kidney. Renal function during chronic hydronephrosis (mean ± SE)

| Dog No. | | Length Occl. (days) | Clearance Periods (No.) | $U_I/P_I$ | GFR ml/min | ERPF ml/min | $\frac{ERPF}{GFR}$ | $U_{Na}/P_{Na}$ | $U_K/P_K$ | $(C_{Na}/GFR) \times 100$ | $(C_K/GFR) \times 100$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 50 | Non-infected | 6 | 8 | 15.3± 6.1 | 53.5± 8.1 | 143±27 | 2.7±0.2 | 0.02±0.02 | 1.77±2.07 | 0.1±0.03 | 6.4± 2.2 |
| 51 | | 6 | 7 | 31.8±30.2 | 59.8± 5.9 | 149±22 | 2.5±0.3 | 0.59±0.30 | 4.29±3.10 | 2.2±1.40 | 17.0± 8.8 |
| 52 | | 7 | 5 | 4.4± 0.9 | 13.9± 5.6 | 88±46 | 6.1±1.0 | - | - | - | - |
| 58 | | 8 | 7 | 4.6± 2.0 | 14.4± 1.5 | 41±14 | 2.7±0.5 | 0.04±0.02 | 0.61±0.21 | 1.3±1.0 | 15.7± 7.3 |
| 60 | | 34 | 5 | 7.6± 3.1 | 27.1± 3.9 | 75± 8 | 2.8±0.4 | - | - | - | - |
| 63 | | 34 | 9 | 20.5±13.7 | 53.2±10.4 | 153±42 | 2.9±0.3 | 0.05±0.02 | 1.3±1.00 | 0.2±0.1 | 41.4± 6.0 |
| 53 | Infected | 8 | 6 | - | - | - | - | - | - | - | - |
| 54 | | 8 | 7 | 2.8± 0.8 | 2.0± 0.7 | 21± 9 | 10.1±0.8 | 0.55±0.09 | 3.40±0.70 | 21.0±5.0 | 125.0±26.0 |
| 55 | | 7 | 7 | 3.3± 1.2 | 8.4± 3.4 | 63±18 | 7.8±1.4 | 0.42±0.04 | 4.10±1.50 | 14.4±5.0 | 126.0±15.0 |
| 56 | | 12 | 8 | 7.4± 1.7 | 27.1± 0.8 | 106±17 | 3.9±0.6 | 0.25±0.04 | 2.20±0.60 | 3.4±0.5 | 29.0± 3.0 |

I = Iothalamate, Na = sodium, K = potassium, U = urine concentration, P = arterial plasma concentration, C = clearance, GFR = clearance of iothalamate, ERPF = clearance of o-iodohippurate

Suki et al. (21) demonstrated that the ascending limb is intact, since solute-free water clearance corrected to the glomerular filtration rate (GFR) was actually greater on the hydronephrotic than on the control side. This difference was attributed to overperfusion of the residual nephrons of the hydronephrotic kidney. The reduction in the functioning nephrons results in a decrease in the amount of sodium transported into the interstitium and, therefore, in reduced meduallary tonicity. This results in a decrease in free water back-diffusion out of the collecting duct and leads to impaired urinary concentrating ability (5).

The pathophysiological process of nephron destruction is believed to be the consequence of a combination of pressure necrosis and ischemic atrophy. Elevated pressure is immediately and directly transmitted to intratubular, precapillary, and interstitial spaces, as verified by micropuncture studies (6).

The increasing volume of the pelvic contents and the collecting system as found in this study and elsewhere (27) has been demonstrated to cause characteristic changes in the renal vasculature (18, 24). Vascular compression, therefore, has also been considered to play a part in parenchymal damage. This is supported by the findings of Vaughan et al. (24), who demonstrated an immediate increase in blood flow upon ureteral release in all animals studied, even after 8 weeks of ureteral occlusion. However, the fall in intrapelvic pressure within 24 h of ureteral occlusion, as shown by these authors, did not correspond to an increase of renal blood flow. Therefore it is apparent that a state of increased renal vascular resistance is attained which is not dependent on a chronic elevation of ureteral pressure. The renal metabolic response to lowered blood flow subsequent to chronic ureteral occlusion is a decrease in oxygen consumption and an increase in anaerobic metabolism (28).

### Rate of Turnover in the Occluded Renal Pelvis

Reabsorption from the renal pelvis is essential for continuous renal function following total ureteral occlusion. Backflow from the renal pelvis in experimental chronic hydronephrosis for 2 to 7 days has been demonstrated (12). These authors could show no difference in the route of backflow between the acute and the chronic preparations (12, 17). The amount of urine entering and leaving the occluded renal pelvis, i.e., the "urine flow", did not differ very much in our experiments from former experiments in acute hydronephrosis (15), where it was found to be 0.06 ml per min on an average. In group 1 the amount of turnover seemed to be slightly greater than in the acute preparation. This may support Hinman's theory (8) that once backflow is established, progressively less and less back pressure is required to maintain it. Taking everything into consideration, the amount of turnover in the occluded renal pelvis seems to be a fairly constant factor. Therefore renal function depends mainly on maintenance of concentration ability.

### The Role of the Lymphatics

It is well established that renal lymph flow increases during ureteral obstruction. (7, 15, 22). This is due to elevation of intrarenal venous pressure rather than to reabsorption from the renal pelvis (7, 1, 15). In subcapsular lymph no reabsorbed urine at all could be demonstrated in acute hydronephrosis, and only approximately 0.3% of the hilar lymph represented reabsorbed urine (15). In chronic hydronephrosis no studies have been made so far.

Our experiments show that none of the urinous substances investigated exceed the arterial plasma concentration in subcapsular lymph. Since the measured urine concentration of iothalamate and o-iodohippurate was found to be greater than the arterial plasma concentration only in group 1, a sufficient amount of renal content reabsorbed into lymph would result in a concentration exceeding unity. In addition, the relative lymph ratios of o-iodohippurate to those of iothalamate are in the same range as in freely draining kindeys (15). Since the concentration ratios in urine of these 2 clearance substances are quite opposite, a change in the ratio in lymph would indicate pyelolymphatic reabsorption. This, in fact, takes place in hilar lymph, but not in subcapsular lymph. In groups 2 and 3 the results are more uniform. The urine concentration of neither iothalamate nor o-iodohippurate exceeded the arterial plasma concentration, but the clearance of o-iodohippurate still exceeded that of iothalamate. The converging subcapsular and hilar lymph concentrations of these 2 substances may point to pyelolymphatic reabsorption in both lymphatic systems. Another explanation seems to be more likely. Since renal lymph can be considered as a filtrate of the intrarenal veins (1), concentrations of substances filtered by the glomeruli and/or secreted by the tubules would be less than corresponding arterial plasma concentrations. In group 2 (4 weeks of hydronephrosis) and especially in group 3 (infected hydronephrosis), GFR and ERPF decreased to minimal amounts and became insignificant as compared with total renal plasma flow, thus not influencing lymph concentration. The high protein content in subcapsular as well as in hilar lymph of infected hydronephrosis may indicate reabsorption of purulent renal pelvic content or more likely changes of permeability in small venules and/or capillaries. This, however, cannot be clarified by our experimental setup.

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