Micropuncture Study of Pressures in Proximal Tubules and Peritubular Capillaries of the Rat Kidney and Their Relation to Ureteral and Renal Venous Pressures\textsuperscript{1,2}

CARL W. GOTTSCHALK AND MARGARET MYLLE

From the Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina

ABSTRACT

Methods are described for direct measurement of the hydrostatic pressure in the surface tubules and capillaries of the rat kidney. In fifty-six anesthetized rats intratubular pressure averaged $13.5 \pm 2.4$ mm Hg. Subsequent microdissection showed that all of the 112 puncture sites so localized were in the first two-thirds of the proximal convoluted tubule. Under all conditions studied, intratubular pressure and the pressure in the peritubular capillaries were approximately the same. Intravenous injection of hypertonic dextrose solution generally produced a brief rise in intratubular and peritubular capillary pressures, which returned to their preinjection levels while the diuresis so produced continued, although at less than the maximal rate. Obstruction of the ureter of kidneys undergoing diuresis resulted in a prompt rise in intratubular pressure, which agreed closely with the simultaneously determined ureteral pressure. Elevation of the ureteral pressure with a pressure bottle had no effect on intratubular or peritubular capillary pressures until it exceeded the pre-existing intratubular and peritubular capillary pressures, and then all rose together up to a maximum intratubular pressure above which elevation of ureteral pressure resulted in no further rise in intratubular or peritubular capillary pressure. Elevation of applied ureteral pressure in kidneys with collapsed tubules and in dead animals did not increase the intratubular pressure, demonstrating that the rise in intratubular pressure produced in this manner in functioning kidneys was not simply a direct back transmission of pressure. Elevation of renal venous pressure by compression of the renal vein also had no effect on intratubular and peritubular capillary pressures until their pre-existing values were exceeded, and then all three pressures rose together.

A KNOWLEDGE of the pressures and their relationship in the vascular and tubular systems of the kidney is essential to an understanding of renal function. Hayman \textsuperscript{(1)} measured the systolic afferent arteriolar and glomerular capillary pressures in the frog and found them to average 85 and 54\%, respectively, of the systolic aortic pressure. In 19 glomeruli with ‘fair to excellent’ circulation in 16 Necturi, White \textsuperscript{(2)} found the glomerular capillary pressure to range from 8.5–27 cm H$_2$O. The pressure in Bowman’s capsule in this same series ranged from 0.1–2.8 cm H$_2$O, and the serum colloid osmotic pressure, 6.5–14.2 cm H$_2$O. It is not permissible, however, to transfer directly pressures from the amphibian kidney, with its low perfusion pressure, to the mammalian kidney.

Winton \textsuperscript{(3)} analyzed the relations between arterial, venous and ureteral pressures in the isolated, perfused dog kidney and formulated the concept of the intrarenal pressure. Walker and Oliver \textsuperscript{(4)} noted that the pressure in the tubules of rats may be ‘very high’ during the infusion of hypertonic sucrose solutions, but

\textsuperscript{1} Received for publication October 3, 1955.
\textsuperscript{2} Supported in part by grants from the Edgecombe-Nash (N.C.) Heart Association, the North Carolina Heart Association, and Public Health Service Grant HT-5033.
they present no measurements of intratubular pressure. More recently, several groups (5-9) have measured the intrarenal or renal interstitial pressure with a needle thrust directly into the substance of the kidney. However, all of these studies are subject to the criticism that they inevitably cause a certain amount of damage to the kidney structure, and precisely what pressure or pressures are measured is not clear. Accordingly, this micropuncture study of the hydrostatic pressures in individual nephrons and capillaries of the rat kidney was undertaken. Since most of the present data were obtained, Wirz (10) has reported that the pressure in the proximal tubules of 17 anesthetized male rats ranged from 9-22 mm Hg and averaged 14.8 mm. In five of these animals, postglomerular capillary pressure was 17.4 ± 2.6 mm Hg. The similarity of these results to our own control pressures is striking.

METHODS AND PROCEDURE

Male albino rats of the Wistar strain, ranging in weight from 150-170 gm and averaging 283 gm, were anesthetized with intraperitoneal sodium pentobarbital, 0.035 gm/kg of body weight. Animals were allowed free access to water and food until the time of the experiment. The left kidney was exposed through a midline abdominal incision with a lateral extension and the animal was placed, back down, on a thermostatically controlled, heated animal board. The viscera were withdrawn to the right and covered with a gauze sponge, kept moist with Ringer's solution. An adjustable barrier, attached to the animal board, was secured between the diaphragm and the left kidney in order to reduce the transfer of respiratory movements to the latter. The surface of the kidney was illuminated with a Knisely quartz rod apparatus and was kept constantly bathed in Ringer's solution heated to 37°C.

Arterial pressure was measured in either the right carotid or femoral artery with a strain gage pressure transducer or capacitance manometer. When mean pressure was not recorded through a suitably damped manometer system, it has been calculated as equal to diastolic pressure plus one-third of the difference between systolic and diastolic pressures. The left external jugular vein was catheterized for intravenous injections and a tracheotomy performed to facilitate tracheal aspiration. When it was desired to study the effect of ureteral pressure, a blunted 22 or 26-gauge hypodermic needle was inserted in the upper one third of the ureter and securely tied with the tip of the needle close to or in the pelvis of the kidney, in order to assure free transmission of pressure from the ureter into the pelvis. The needle was attached by polyethylene tubing filled with Ringer's solution to a strain gage pressure transducer for measuring ureteral pressure or to a pressure bottle when it was desired to study the effects of various applied ureteral pressures. Urine flow was measured by allowing the urine to drip out of the end of the plastic tubing onto a strain gage force transducer, and the rate of dropping was recorded electronically. Renal venous pressure was measured with a 22-gauge needle with one lateral hole near its tip inserted into the renal vein and also attached by Ringer-filled polyethylene tubing to a strain gage pressure transducer. The zero level for arterial, venous and ureteral pressures was the same as zero intratubular pressure which was determined by the tip of the micropipette used to measure the intratubular pressure.

To measure intratubular pressure, a micropipette 6-10 μ outside diameter at its tip was filled with a concentrated aqueous solution of filtered methylene blue or nigrosin. The pipette was clamped in a de Fonbrune micromanipulator receiver which had been mounted on an adjustable microscope stand with a horizontal arm for greater freedom of movement. The micropipette was connected by air-filled polyethylene tubing to a pressure bottle and mercury manometer. The micropipette was manipulated into the fluid on the kidney surface and, using a stereoscopic binocular microscope at 150 X magnification, its capillarity was determined. Capillarity was recorded as equal to that pressure which had to be applied to the pipette so that dye did not leave nor fluid enter it. Capillarity, generally 1-3 mm Hg, was checked frequently during each experiment and did not change more than 1 mm in any pipette. The pipette was then maneuvered with the fine adjustment of the manipulator until its tip entered the lumen of a surface tubule, as evidenced by the surge of clear fluid into it. The intratubular pressure was recorded as equal to that pressure which had to be applied to the pipette in order to keep dye from leaving the tip and tubular fluid from entering it, minus the capillarity of the pipette. In general, it proved sufficient to find two pressures differing by no more than 2 mm Hg which produced inflow and outflow. Intratubular pressure could then be determined to the nearest millimeter of mercury, and the observer could be certain that the tip of the micropipette was freely open and not impinging on the tubule wall. The injected dye was carried away rapidly by the tubular fluid and usually returned briefly to the surface of the kidney a few moments later in a more distal convolution of the proximal tubule or in a convolution of the distal tubule. Injection of dye into the tubule also made clearly evident any leak which might occur at the site of puncture, for then dye could be seen streaming out of the tubule around the microtip. Leaks were most frequent when the intratubular pressure was high.

At times, there was sufficient motion of the kidney synchronous with respiration that intratrabecular administration of oxygen with or without 0.5 μ of tubocurarine chloride intravenously was required to abolish the excursions. The majority of the experiments have been done without tubocurarine. In addition to respiratory movements, there was also a slight and rapid expansile pulsation of the kidney, presumably synchronous with heart beat. When this was troublesome, it was easily obliterated by very slight downward pressure with the quartz rod.

The great majority of the intratubular pressures measured were those of surface tubules. When the
kidney was flaccid, however, the force required to manipulate the pipette through the capsule often drove it several layers deep into the kidney substance. No reading was accepted, however, unless it could be consistently repeated several times. Pressures in the peritubular capillaries were measured in a similar manner, but with greater difficulty due to their smaller size. Micropipettes with tips sufficiently large to permit free entrance and exit of red cells were used.

To determine the site of puncture, a modification of the method of Walker and Oliver (4) was employed. After measuring the pressure the tubule was filled with nigrosin, the kidney was removed, decapsulated, and macerated in 50% hydrochloric acid at 37°C for 13 hours. The tissue was then washed thoroughly in tap water, and the marked nephron dissected out under a stereoscopic binocular microscope at 27 X magnification and the point of entrance of the pipette identified. As the punctures were all localized in the proximal tubules, only these were dissected out, simplifying the procedure a great deal. The distance of the puncture site from the glomerulus and the entire length of the proximal tubule were measured with a micrometer eyepiece as described by Wirz and Bott (12).

**OBSERVATIONS**

**Appearance of the Kidney.** The kidney presented an appearance similar to that described by Walker and Oliver (4). The entire surface was a mass of short segments of tubules surrounded by capillaries. Detail of visualization of tubules and capillaries was excellent, and the tubules had distinct lumina well-distended with colorless fluid. Circulation in the peritubular capillaries was brisk. Certain capillaries were considerably larger than the majority of the others and apparently corresponded to the postglomerular capillaries described by Wirz (10). Very rarely, glomeruli were visible and appeared as hemispherical elevations on the surface. The glomeruli were too indistinct, however, to permit micropuncture or critical observation of their circulation.

Injection of hypertonic glucose solution and increase in ureteral pressure produced a noticeable increase in the diameter of the tubular lumina and in kidney size. Venous congestion, on the other hand, resulted in an increase in the size of the kidney and in the diameter of the peritubular capillaries and compression of the tubules. Rapid but slight pulsation of injected dye, presumably synchronous with heart rate, was especially evident at high intratubular pressures.

Collapse of all or a portion of the visible tubules sometimes occurred after accidental trauma to the animal, i.e., hemorrhage or anoxia, and rarely without demonstrable cause. The collapsed tubules appeared white and opaque, and their lumina were more or less completely obliterated. A similar appearance of the other and previously unexposed kidney proved that this was not due to local trauma to the exposed kidney. When only a portion of the tubules collapsed, small groups of distended tubular segments were surrounded by collapsed segments. Attempts to measure the pressure in some of the former met with little success for two reasons. In the first place, these kidneys were always very soft, and the tip of the pipette would plunge deep into the kidney through several layers of tubules. Secondly, although the tubules were filled with fluid, there was, at most, sluggish flow in them, making it difficult to measure the intratubular pressure. The few measurements obtained suggested that the intratubular pressure was very low, 5 mm Hg or less, under such conditions. Except where otherwise stated, all observations herein reported were made on kidneys with well-distended tubules. Collapsed tubules are believed to represent an abnormal state.

**Control Intratubular Pressure.** In the exposed but otherwise unmanipulated kidneys of 56 rats, the pressure in 193 tubules ranged from 7-21 mm Hg and averaged $13.5 \pm 2.4$ mm Hg. The 95% confidence interval for the average intratubular pressure was from 13.1-13.8 mm Hg. The average intratubular pressure for each rat also ranged from 7-21 mm Hg and averaged $13.3 \pm 3.0$ mm Hg. The intratubular pressure was the same in the 13 animals that received tubocurarine and oxygen as in the 43 that did not.

As long as the experimental conditions remained unchanged, repeated measurement of the intratubular pressure at the same puncture site demonstrated that it would either remain constant or vary over a range of several millimeters of mercury. When the pressure was measured in two or more tubules in the same kidney, the standard deviation was 2.4 mm Hg.

The intratubular pressure was the same when measured without injection of dye by maintaining the fluid-dye interface at a constant location in the tip of the micropipette as when measured by finding two pressures

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Standard deviation.
differing by no more than 2 mm Hg which produced inflow and outflow of minute amounts of dye and tubular fluid. Moreover, injection of much larger quantities of dye than employed in measuring the intratubular pressure had no demonstrable effect on the pressure in the tubule, and the dye was rapidly swept away by the tubular fluid.

Site of Tubule Puncture. After measuring the pressure in 112 nephrons in 20 animals, the site of puncture was identified as described above. In all instances, proximal convoluted tubules had been punctured. The site of puncture varied from .1-.66 of proximal tubule length when expressed as a ratio of the distance from glomerulus to puncture site divided by the total length of the proximal tubule in the 46 nephrons in which the latter was measured. In 20 of the 46 nephrons, the puncture was located in the middle one-third of the proximal tubule.

Relation of Intratubular Pressure to Distance From Glomerulus and to Length of Proximal Tubule. In an effort to gain information about the pressure required to produce flow down the tubule, the intratubular pressure was compared to the distance of the puncture site from the glomerulus. In the 88 nephrons isolated after measuring the intratubular pressure under control conditions, there was no correlation between the intratubular pressure and the distance from the glomerulus.

The total length of the proximal tubule was measured in 46 nephrons and varied from 6.0-10.1 mm with an average of 7.7 mm. There was no correlation between the intratubular pressure and the total length of the proximal tubule in this group.

Relation of Control Intratubular Pressure to Arterial Pressure and Body Weight. Mean arterial pressure was measured in 46 of the control animals and averaged 118 ± 21 mm Hg. There was no correlation between control intratubular pressure and body weight or arterial pressure and body weight.

Relation of Intratubular Pressure to Peritubular Capillary Pressure. The pressure in peritubular capillaries was measured in 12 rats of the control series and 9 of the Ringer’s series (see below) before the kidneys had been otherwise manipulated, and the results are presented in table 1. The intratubular pressure was identical with the pressure in the small peritubular capillaries, while the pressure in the large peritubular capillaries was significantly higher.

Intratubular and peritubular capillary pressures also agreed closely (fig. 1) when they were elevated by intravenous injection of 20% dextrose solution, venous compression, or applied ureteral pressure. As shown, the pressure in the large peritubular capillaries generally slightly exceeded the intratubular pressure at all pressure levels, while the pressure in the tubules and small peritubular capillaries agreed closely at all pressure levels.

Effect of Parenteral Fluid Administration on Intratubular Pressure and Its Relation to Urine Flow. The intratubular pressure was measured in an additional 21 rats that were given 5 ml of Ringer’s solution subcutaneously following induction of anesthesia. The intratubular pressure ranged from 11-22 mm Hg in 52 tubules and averaged 14.6 ± 2.4 mm Hg. Although the difference is small, statistically it is significantly different from the intratubular pressure of the control group at the 1% level. The 95% confidence interval of the Ringer’s series was 13.9-15.3 mm Hg. The average intratubular pressure for each rat ranged from 11-21 mm Hg and averaged 14.5 ± 3.0 mm Hg.

The mean arterial pressure was measured in 19 of these animals and averaged 128 ± 18 mm Hg, which is not significantly different from the average mean arterial pressure of the control group. Again, there was no correlation between arterial pressure and intratubular pressure.
The rate of urine flow was measured in eight rats, four in the control series and four in the Ringer’s series, and averaged 1 drop every 13 and 12 minutes, respectively. (One drop = 0.02 ml) Following the intravenous injection in 1 minute or less of 1–2 ml of 20% dextrose solution, the intratubular pressure was observed to rise in 13 out of 15 trials in eight animals. The increase in intratubular pressure varied from 5–25 mm Hg and averaged 11 mm. The experiment with the most marked rise in intratubular pressure is shown in figure 2. The rate of urine flow increased after each injection of dextrose, reaching peak flows of 1–10 drops/min. and averaging 7.5 drops/min. Although the intratubular pressure fell to its preinjection value in 4–19 minutes, average 7.5 minutes, the diuresis continued but at less than the maximal rate. Accordingly, there was no close correlation of intratubular pressure and rate of urine flow, as was also reported by Wirz (10). Following a momentary fall during the injection (fig. 2), the arterial pressure usually increased after dextrose, but the blood pressure response was very variable and there was no correlation between intratubular pressure and arterial pressure.

Peritubular capillary pressures were also measured in these eight rats and always agreed closely with the simultaneous intratubular pressure. There were no consistent differences in the response of the animals pretreated with Ringer’s solution as compared to the rats that did not receive Ringer’s solution.

**Effect of Ureteral Occlusion.** In 11 rats, the left ureter was connected by polyethylene tubing filled with Ringer’s solution to a strain gage pressure transducer for intermittent measurement of ureteral pressure. In four animals that had received no parenteral fluids, five periods of ureteral occlusion lasting from 6–11 minutes resulted in a rise in ureteral pressure towards the pre-existing intratubular pressure but with little elevation of the latter. In nine kidneys undergoing diuresis, however, ureteral occlusion resulted in a rapid rise of both ureteral and intratubular pressures. A typical experiment is illustrated in figure 3. During urteral occlusion, there was close correspondence of intratubular and ureteral pressures up to the highest pressures observed, 88 mm Hg, as shown in figure 4, with the intratubular pressure generally slightly exceeding the ureteral pressure. When intratubular pressure and ureteral pressure had reached a steady state, a change in arterial pressure resulted in a similar change in ureteral pressure, as noted in earlier studies of the ‘maximum ureteral pressure’ (13). In one experiment, a marked and persistent fall in arterial pressure occurred while the intratubular and ureteral pressures were elevated. The latter pressures fell almost simultaneously, and the intratubular pressure was lower than the ureteral pressure until the ureteral obstruction was removed. When the ureter was again occluded, intratubular pressure exceeded ureteral pressure as usual. In the presence of ureteral obstruction, intravenous injections of hypertonic dextrose solution resulted in a marked and prompt rise in intratubular and ureteral pressures, and such injections are the cause of the high pressures recorded in figure 4. In a typical experiment, within 4 minutes following 1 ml of 20% dextrose, the intratubular pressure rose from a pre-injection value of 16–50 mm Hg, while the ureteral pressure rose from 11–40 mm Hg. Mean arterial pressure increased 10 mm Hg.

**Effect of Applied Ureteral Pressure.** In 10
animals the left ureter was connected to a Ringer's-filled pressure bottle so that the pressure in the ureter could be adjusted to any desired value. As shown in figure 5, an increase in applied ureteral pressure had no effect on intratubular pressure until it it exceeded the pre-existing intratubular pressure, and then both rose together, with the intratubular pressure generally 1-3 mm Hg higher than the ureteral pressure. In five rats intratubular and ureteral pressures corresponded closely up to the maximal ureteral pressures employed, which ranged from 28-37 mm Hg. In the other five rats, in three of which peritubular capillary pressures were also measured, an upper limit of agreement of intratubular and peritubular capillary pressures with ureteral pressure was found above which elevation of ureteral pressure resulted in no further rise in the former pressures. Four of these animals received no parenteral fluids, and the upper limit of intratubular and peritubular capillary pressures was between 35 and 40 mm Hg. The fifth rat received 2 cc. of 20% glucose intravenously, and intratubular and peritubular capillary pressures equalled or slightly exceeded the ureteral pressure up to 50 mm Hg, but fell to 35 and 40 mm when the ureteral pressure was raised to 55 and 60 mm Hg, suggesting intrarenal vasoconstriction with these high ureteral pressures. In those experiments where an upper limit of intratubular pressure was found, the flow in the tubules appeared to slow at that point, and the injected dye could be seen collecting in them. In all 10 rats the intratubular pressure fell correspondingly when an elevated ureteral pressure was reduced. A change in intratubular pressure subsequent to a change in ureteral pressure usually occurred within 1 minute, and the intratubular pressure was then constant until the ureteral pressure was again changed. At any given increase in applied ureteral pressure, the intratubular pressure appeared to be uniform throughout the kidney.

In dead animals and in kidneys with collapsed tubules, an increase in applied ureteral pressure did not result in an increase in intratubular pressure.

Relation of Intratubular and Peritubular Capillary Pressures to Renal Venous Pressure. In six animals, intratubular and peritubular capillary pressures were measured while the renal vein was constricted to varying degrees with a ligature. As shown in figure 6, the results were similar to the effects of applied ureteral pressure, except that at all levels of increased renal venous pressure studied, intratubular and peritubular capillary pressures corresponded closely to the renal venous pressure. However, at the very high levels of venous pressure, fluid movement in the tubules was slow or absent, suggesting that glomerular filtration had been greatly reduced or abolished. When the venous pressure was lowered, intratubular and peritubular capillary pressures were correspondingly reduced. A change
in the latter pressures secondary to a change in renal venous pressure occurred as rapidly as the intratubular and peritubular capillary pressures could be measured, approximately 1 minute, and did not change significantly until the venous pressure was again altered. The scatter of the data is greater than in the applied ureteral pressure experiments, and this difference is due, at least in part, to the greater difficulty in maintaining a constant elevation of renal venous pressure for time periods sufficiently long to measure intratubular and peritubular capillary pressures.

DISCUSSION

It may be assumed that the intratubular pressures measured in this study were pressures in the proximal tubules, as all of the 112 puncture sites identified were in this segment of the nephrons. Similar experience was reported by Walker and Oliver (4), and Wirz and Bott (12). The pressures found in the tubules and peritubular capillaries in these experiments agreed remarkably well with those reported by Wirz (10). Our mean intratubular pressure for 56 rats was 13.5 ± 2.4 mm Hg, and Wirz', 14.8 ± 2.6 mm Hg in 17 rats. There was a similar correspondence between the smaller series of peritubular capillary pressures.

It may be questioned whether the introduction of the microtip significantly changed the intratubular pressure. Barring leaks, which were easily detected, this seems highly unlikely for several reasons. In the first place, the external diameters of the microtips, 6–10 μ, were small compared to the internal diameters of the tubules, which were estimated to be at least 20 μ or more under control conditions and approximately 35 μ at higher intratubular pressures. At all pressure levels, rapid flow continued down the tubule around the tip save in those instances already mentioned with ureteral and venous obstruction. The close correspondence of intratubular and peritubular capillary pressures under all conditions studied is also strong evidence that the tips did not significantly alter dynamics in the tubule, for there is such a rich anastomotic peritubular capillary network that even total obstruction of a capillary is not likely to produce any significant change in the network itself. Additional evidence for the validity of the methods is the close correspondence of intratubular and ureteral pressures. The ureteral pressures of obstructed kidneys represent pressures contributed to by all the nephrons, only an insignificant number of which were punctured. That the injection of the quantities of dye used to measure pressure did not change the intratubular pressure is proved by the fact that the intratubular pressures were the same when they were determined by maintaining the fluid-dye interface at the same location in the pipette tip without injection of dye and the fact that injection of much larger quantities of dye than ordinarily employed did not alter the intratubular pressure.

Pressure Interrelations. As clearly foreseen by Ludwig (14), these experiments conclusively demonstrate that a pressure change in the venous system is transmitted to the tubules and that a pressure change in the tubules is transmitted to the peritubular capillaries so that the pressures in the tubules and peritubular capillaries were approximately the same under all conditions studied. The rise in peritubular capillary pressure with an increase in ureteral pressure is apparently due to compression of intrarenal veins or venules by the dilated tubules. The failure of applied ureteral pressures to increase the intratubular pressure in kidneys with collapsed tubules and in dead animals is strong evidence that the rise in intratubular pressure. Barring leaks, which were easily detected, this seems highly unlikely for several reasons. In the first place, the external diameters of the microtips, 6–10 μ, were small compared to the internal diameters of the tubules, which were estimated to be at least 20 μ or more under control conditions and approximately 35 μ at higher intratubular pressures. At all pressure levels, rapid flow continued down the tubule around the tip save in those instances already mentioned with ureteral and venous obstruction. The close correspondence of intratubular and peritubular capillary pressures under all conditions studied is also strong evidence that the tips did not significantly alter dynamics in the tubule, for there is such a rich anastomotic peritubular capillary network that even total obstruction of a capillary is not likely to produce any significant change in the network itself. Additional evidence for the validity of the methods is the close correspondence of intratubular and ureteral pressures. The ureteral pressures of obstructed kidneys represent pressures contributed to by all the nephrons, only an insignificant number of which were punctured. That the injection of the quantities of dye used to measure pressure did not change the intratubular pressure is proved by the fact that the intratubular pressures were the same when they were determined by maintaining the fluid-dye interface at the same location in the pipette tip without injection of dye and the fact that injection of much larger quantities of dye than ordinarily employed did not alter the intratubular pressure.

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tubular pressure produced by an increase in applied ureteral pressure is not simply a direct back transmission of pressure. As suggested by Cushny (15), an unopposed ureteral pressure probably results in flattening of the papilla of the kidney and obstruction of the openings of the tubules into the pelvis. In the functioning kidney, an increase in applied ureteral pressure produces an obstruction to the outflow of urine, and thus a rise in intratubular pressure, as shown in figure 5, towards the glomerular capillary pressure, reducing the effective filtration pressure and the glomerular filtration rate. But the intratubular pressure cannot exceed a value equal to the glomerular capillary pressure minus the effective (plasma minus tubular fluid) colloid osmotic pressure, at which point filtration would cease. As discussed by Winton (3), tubular reabsorption and hence glomerular filtration at a reduced rate would presumably continue until the character of the solutes remaining in the tubular fluid is such that further active reabsorption is impossible. At this point, the fluid in the tubule would be motionless. The glomerular capillary pressure, however, may have been elevated during this course of events above its preobstruction value by the increase in peritubular capillary pressure resulting from the increased intratubular pressure. The finding in four experiments that the intratubular pressure and peritubular capillary pressure could not be raised above 35-40 mm Hg by increasing the applied ureteral pressure, and the apparent diminution of flow in the tubules at these pressures suggest that filtration equilibrium was approximated in these experiments. If the colloid osmotic pressure is taken to be 25 mm Hg and if the tubular fluid was essentially protein free, this suggests that the glomerular capillary pressure under these conditions was approximately 60-65 mm Hg or 50% of the arterial pressure. The relationship of this value to the glomerular capillary pressure in unobstructed kidneys is not certain, and it may be higher for reasons discussed above. On the other hand, high applied ureteral pressures may result in intrarenal vasoconstriction and a fall in glomerular capillary and intratubular pressures, as apparently occurred in one experiment.

Our findings of the relationship of renal venous pressure to intratubular pressure correspond closely to Winton's (3) analysis of the effects of increased renal venous pressure, but our studies of the effects of applied ureteral pressure do not support his explanation of the difference in ureteral and venous pressures required to produce equal reductions of urine flow when applied one at a time. Winton postulated that an increase in ureteral pressure increased the intratubular pressure but not the glomerular capillary pressure, in contrast to an increase in venous pressure which was thought to do both. The fact that an in-

![Fig. 5. Relation between intratubular and peritubular capillary pressures and applied ureteral pressure. Peritubular capillary pressures were measured in 3 rats and intratubular pressures in all 10 animals.](http://ajplegacy.physiology.org/doi/abs/10.220.33.2)
crease in both ureteral and venous pressures produces a corresponding increase in peritubular capillary pressure suggests that an increase in glomerular capillary pressure is as likely to occur with the one as the other, although not necessarily to the same degree, which could account for the difference in ureteral and venous pressures required to produce equal reductions of urine flow. Moreover, it is possible that the efferent arterioles are so distensible that a rise in peritubular capillary pressure will have no effect on glomerular capillary pressure until it exceeds the pre-existing glomerular capillary pressure, just as an increase in renal venous and ureteral pressures does not affect intratubular and peritubular capillary pressures until the pre-existing pressures are exceeded. This does not seem likely, however, and the finding at all pressure levels that the pressure in the large and presumably postglomerular capillaries exceeded the pressure in the smaller peritubular capillaries (fig. 1) also suggests that this is not the case. Winton's finding of a difference in ureteral and venous pressures required to produce a similar reduction in urine flow could also be related to the fact that an increase in ureteral pressure dilates the tubules, while an increase in venous pressure compresses them or to an effect on tubular reabsorptive mechanisms. The peritubular capillaries appear to be dilated under both circumstances. In addition, an increase in venous pressure in the presence of a similar and previous increase of ureteral pressure may temporarily increase the urine flow by compressing the dilated tubules and partially emptying them of fluid.

**Pressure Gradient in the Proximal Tubule.** The pressure required to produce flow of the low viscosity fluid down the tubules is unknown, but the lack of correlation between the intratubular pressure and the distance of the puncture site from the glomerulus suggests that the proximal tubules offer relatively little resistance to flow, as Gómez (16) has concluded. The apparent low resistance of the proximal tubule probably also accounts for the lack of correlation between its length and intratubular pressure. The thin limb of the loop of Henle, no doubt, offers a greater resistance to flow, but much of the tubular fluid is already reabsorbed when this segment is reached. By using the data available for the glomerular filtration rate and number of glomeruli in the rat, the pressure required for flow of the filtrate along hypothetical tubules of various sizes can be readily calculated, assuming that the flow obeys Poiseuille's law:

\[
\dot{Q} = \frac{8Ql\Delta P}{\pi r^4} = \frac{8 \times 4 \times 10^{-7} \times 1 \times 7 \times 10^{-3}}{\pi \times 1 \times 10^{-12}} = 7130 \text{ dynes/cm}^2 = 5.4 \text{ mm Hg}
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This is the pressure required for the entire filtrate to flow along the tubule, and if 80% of the filtrate is reabsorbed in the proximal tubule (19), the pressure drop in the proximal tubule would be 3.5 mm Hg. If the radius were 12 \(\mu\), a pressure drop of 1.6 mm Hg would occur, and only 0.7 mm Hg if the radius were 15 \(\mu\). Our estimates of tubular size indicate that the radius of the proximal tubule is at least 10 \(\mu\), and probably somewhat more under control conditions and considerably more than this during diuresis and ureteral obstruction. These theoretical considerations indicate that the pressure drop in the proximal tubule is so small as to be undetectable by our present methods. The finding of continuous flow of fluid in all of the tubules punctured under control conditions is believed to be strong evidence against total glomerular intermittency under these conditions. The absence of demonstrable correlation between intratubular pressure and arterial pressure under control conditions does not mean that the intratubular pressure is independent of the arterial pressure, for this, of course, is its source, and studies are in progress in an attempt to define their relationship.

**Hypertonic Glucose Solution.** Although studies of the effects of various diuretic agents
and rates of urine flow on the intratubular pressure are incomplete, it is suggested that the rise in intratubular pressure usually seen following hypertonic glucose solution is due, at least in part, to retention of additional water within the tubular lumen as a consequence of the inability to reabsorb all of the glucose that had been filtered. This could dilate the tubules and obstruct the intrarenal veins or venules and raise the peritubular capillary pressure to a corresponding degree. The latter in turn may result in an increase in glomerular capillary pressure, tending to maintain constant the effective filtration pressure and the glomerular filtration rate. A rise in arterial pressure often accompanied the administration of hypertonic glucose solution and may also be in part responsible for the increase in intratubular and peritubular capillary pressures observed. The increase in arterial pressure cannot be the only cause, however, as the rise in intratubular pressure often exceeded the rise in arterial pressure, especially in the presence of ureteral occlusion.

Renal Interstitial Pressure. The present experiments aid in the interpretation of the previous studies of the intrarenal or renal interstitial pressure in which the pressure in the kidney was measured through a hypodermic needle or small glass cannula plunged into its substance. Such a needle will damage blood vessels, tubules, glomeruli and lymphatics, and the pressure measured is determined by the pressure measured in this manner is probably a reflection of the similarity of pressure in the proximal tubules and peritubular capillaries, which structures constitute the bulk of the kidney mass. Moreover, Swann (20) has found the interstitial pressure to be identical with the pressure measured through small plastic cannulae threaded sufficiently far back into the veins of the kidney through the renal vein.

Our mean control intratubular pressure of 13.5 ± 2.4 mm Hg is slightly higher than the mean interstitial pressure of 10.4 ± 3.0 mm Hg previously reported (6) for 36 rats and obtained under closely similar conditions. The relationship between intratubular and peritubular capillary pressures and venous pressure is identical to the relationship between interstitial pressure and venous pressure (6, 21). Similarly, there is no correlation between control intratubular or interstitial (5, 8) pressures and arterial pressure. The rise in interstitial pressure with osmotic diuretics (7, 8, 22, and unpublished observations) corresponds to the rise in intratubular pressure usually found after hypertonic dextrose solution. A rise in interstitial pressure with applied ureteral pressures was also reported previously (6) and was found to correspond to about one-half of the effect of a similar rise in venous pressure. The present experiments make it clear that the maximum intratubular pressure had been exceeded in the earlier experiments, as ureteral and interstitial pressures differed only at high applied ureteral pressure and corresponded closely at low ureteral pressure.

We are indebted to Dr. Bernard G. Greenberg, Professor of Biostatistics, University of North Carolina, for the statistical analysis of these data. We wish to thank Mr. William Elliott for technical assistance with some of these experiments.

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