J. Physiol. (1955) 129, 436–447

THE BEHAVIOUR OF THE INTACT URETER IN DOGS, RABBITS AND RATS

BY D. W. GOULD, A. C. L. HSIEH AND L. F. TINCKLER
From the Departments of Physiology and Surgery, University of Hong Kong

(*Received* 11 *November* 1954)

To complement the study on the isolated buffalo ureter reported in the preceding paper (Gould, Hsieh & Tinckler, 1955*a*) an investigation has been made on the behaviour of the intact ureter in dogs, rabbits and rats.

METHODS

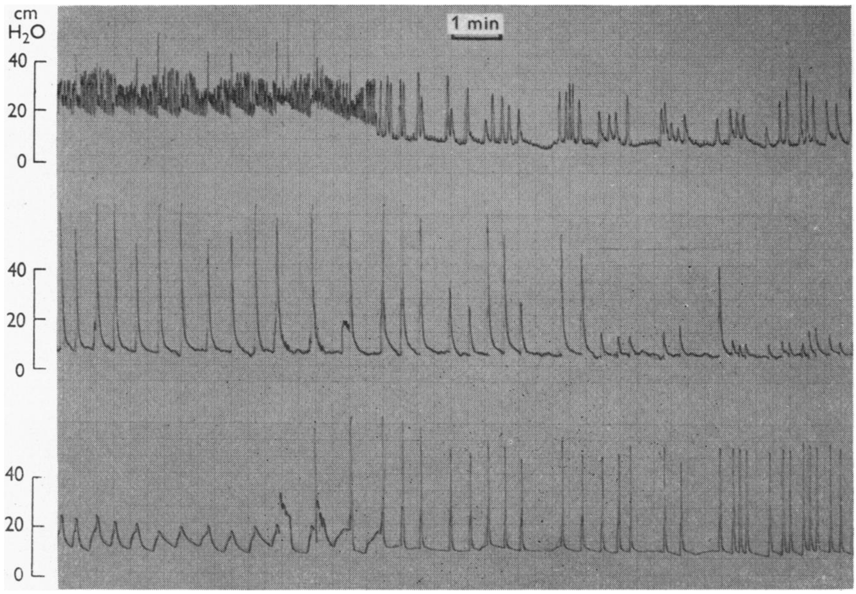
Pressure tracings were made in experiments on sixteen dogs anaesthetized with intravenous sodium pentobarbitone (Nembutal 50 mg/kg). The abdomen was opened by a mid-line incision from top to bottom, and the abdominal contents packed away from one or other ureter. Simultaneous pressure records were obtained from each third of the ureter, or from two points on the ureter and from the bladder. To record pressures from the ureter, hypodermic needles sealed to fine polythene tubing were thrust into the lumen. The tubing was attached to Statham strain-gauge manometers, and these were connected to a Sanborn 'Poly-Viso' physiological recorder. Bladder pressure was recorded from a catheter inserted through the urethra. In four dogs the bladder was opened and the discharge of urine from the ureteric orifice was observed and signalled. When diuresis was required, 5% dextrose solution was given by rapid intravenous drip. Bladder pressure was varied either by manual compression or by emptying and filling by way of a wide-bore needle thrust through the wall. The flow of urine down the ureters of nine dogs, eleven rabbits and two rats were observed after intravenous injection of indigo carmine.

RESULTS

Pressure records from the dog

Pressures recorded from three points on the ureter. Pressure patterns from each of three points were often found to differ sharply from one another, both in respect to basic pressure (that is the pressure existing between peristaltic waves) and in respect to the rise of pressure caused by passage of a peristaltic wave. Basic pressures mostly fell within a range of 0–30 cm water, and wave amplitudes ranged from 4 to 70 cm water. The general pattern of the triple trace also varied greatly between animals, and in the same animal from time to time (Text-fig. 1).

Despite these variations, two main patterns were recognizable. In the first a regular series of peristaltic waves originating at the upper end of the ureter caused a rise in pressure at successive needle points, the pressure at each needle returning to its original level between waves (through pattern). In the second, each of a regular series of waves in the top section produced a small peak and a



Text-fig. 1. Pressure tracings from upper, middle and lower thirds of a dog's ureter in that order from above downwards, showing how basic pressure, and also wave amplitude, form and frequency may vary from part to part and from time to time.

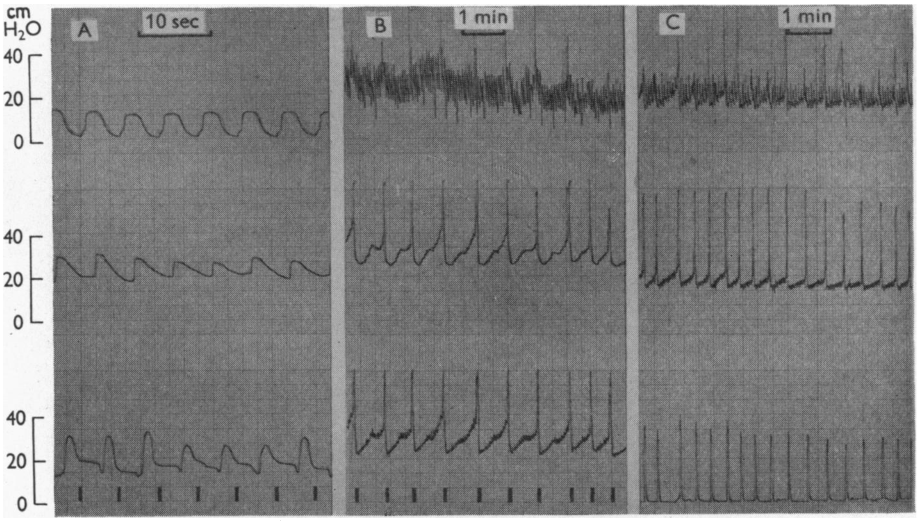
slight rise of basic pressure further down the ureter. When the basic pressure in the lower part reached a certain level, a large contraction occurred in this part, following which the basic pressure fell, and the pattern was then repeated (segmental pattern) (Text-fig. 2).

In the absence of diuresis, basic pressure was often lowest at the upper end and highest at the lower end, but basic pressure was sometimes zero at one, two, or all three needle points.

Effect of diuresis. When a rapid intravenous infusion of 5 % dextrose solution was used to produce diuresis, a segmental pattern was often converted into a through pattern. If, before diuresis, the basic pressure was higher at the bottom end of the ureter than at the top end, the increase in urine flow sometimes reversed this relationship (Text-fig. 3). In general, both basic pressure and frequency and amplitude of waves increased with an increase in urine flow.

A burst of peristaltic activity could always be produced by injecting a little water into the lumen of the ureter through the recording needle.

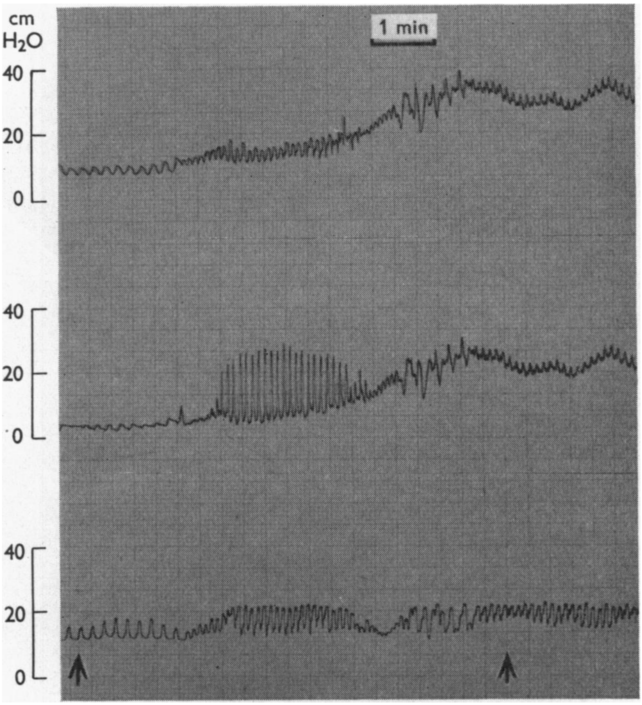
Relationship between wave patterns and discharge of urine from the ureteric orifice. If a ureter showed a segmental pattern, urine escaped from the ureteric orifice only when a large pressure wave occurred in the lower end of the organ. As many as twenty large, even waves might occur in the upper part of the ureter for every large wave at the lower end capable of producing a discharge of urine. When a through pattern was recorded, each wave running from top to bottom of the organ produced a discharge (Text-fig. 2).



Text-fig. 2. Pressure tracings from upper, middle and lower thirds of dog's ureters in that order from above downwards. A and B are from the same dog and the bladder had been opened for discharge of urine to be observed. Vertical dashes mark escape of urine from ureteric orifice. A shows a through pattern, and urine enters bladder with each wave. B shows a segmental pattern, urine being fed into lower two-thirds from upper one-third and entering bladder only with contraction of lower end. C is from another dog showing a segmental pattern, the basic pressure at the lower needle being flat at zero between waves indicating that at this point the ureter is closed except at the passage of a spindle of urine.

Effect upon ureteric activity of altering bladder pressure. Resting bladder pressures were from 5 to 6 cm water. Micturition produced an intravesical pressure of 50 cm water or more. Raising the bladder pressure within this range, either by manual compression or by distension with water, produced an effect on ureteric pressure patterns proportional to the pressure in the bladder and the rate of urine formation. The typical response in the ureteric tracing was a rise in basic pressure and an increase in the height and frequency of the peristaltic waves. The effect was generally greatest in the lower part of the ureter.

In several animals a rise of 10–15 cm water in the basic pressure at the lower end of the ureter occurred without any change in the trace recorded from the upper end. The upper end sometimes showed a smaller and delayed rise in basic pressure, and sometimes an increase in amplitude of peristaltic waves without change of basic pressure (Text-fig. 4).



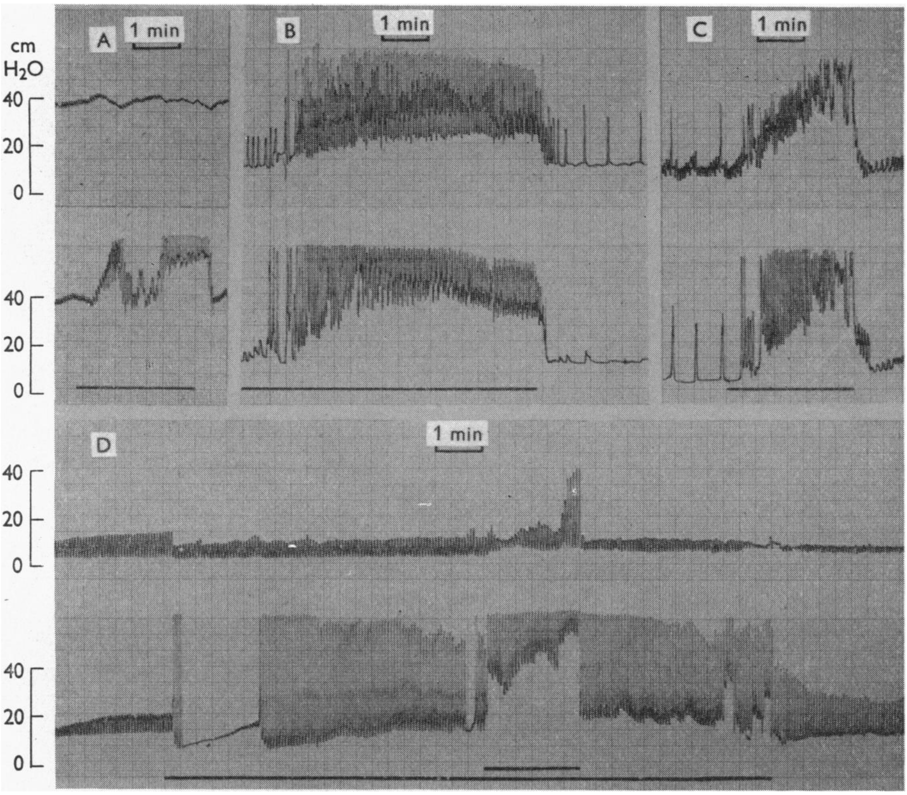
Text-fig. 3. Pressure tracings from upper, middle and lower thirds of a dog's ureter in that order from above downwards. Between the arrows 150 ml. of 5% dextrose was given by rapid intravenous drip, and the heavy diuresis so produced caused a rise in basic pressure in the upper two-thirds of the organ and stimulated peristalsis.

The increase in basic pressure at the lower end occasionally was as high as 40 cm water, but commonly measured about one-fifth of the rise in bladder pressure. It was never sufficient to make ureteric basic pressure and bladder pressure equal.

When urine production was small a rise in bladder pressure maintained for several minutes had only a delayed and mild effect upon the ureter, but when urine was produced rapidly the ureteric response was considerable and immediate.

Placing a bulldog clip on the lower end of the ureter produced the same effect on pressure patterns as a raised bladder pressure, except that a clip always caused basic pressure to rise at all three needle points, and the final pressure attained was the same throughout the organ. A similar picture was obtained if a bladder pressure of 30–50 cm water was produced while the rate of urine production was very high (Text-fig. 4).

We have confirmed the observation of Satani (1919) that it is impossible to cause urine to flow into the ureters from the bladder because of the flap-valve form of the ureteric orifices.



Text-fig. 4. Pressure tracings from upper and lower halves of the ureter in dogs to show the effect upon ureteric activity of a raised bladder pressure. In A the horizontal line marks a period during which the bladder was contracting spasmodically in an attempt to force urine past an indwelling catheter and producing intravesical pressures of over 50 cm water. The signal in B marks a period during which bladder pressure was maintained at 50 cm water by manual compression. C is the same manoeuvre in the same animal a little later during a period of extreme diuresis. In D the single line marks a period during which bladder pressure was raised from 7 to 20 cm water by inflation, and the double line a period during which a 50 cm pressure was maintained by compression.

Observations on the passage of dyed urine along the ureter

No differences were noted between dog, rat and rabbit. Urine travelled from renal pelvis to bladder by two main methods. In the first, spindles of urine periodically appeared at the upper end of the ureter and passed straight down in front of a peristaltic wave to escape into the bladder; in the second, two or more pools of urine formed along the length of the ureter, the pools receiving spindles from above and discharging spindles from their lower ends (Pl. 1, figs. 1–3).

One method would sometimes give way to the other spontaneously, but when urine was travelling straight through in spindles, a pool pattern could always be produced by raising pressure in the bladder or by increasing the rate of urine production.

The common sites for pooling were at the upper end of the ureter immediately below the renal pelvis, and in the lower third of the organ. The lower pool might reach the bladder wall, but often the portion of ureter next to the bladder remained closed. A pool sometimes formed about half-way down the ureter, or the lower pool might occupy the entire lower three-quarters. Occasionally in the rabbit the whole ureter was filled with urine, but this only occurred towards the end of an experiment after the ureter had been exposed for some time. Apart from such occasions, or the complete obstruction of the flow of urine into the bladder, an otherwise full ureter always showed a closed portion, 5–10 mm in length, between a large lower pool and a small upper one (Pl. 1, fig. 4).

The upper pool usually appeared to be continuous with the cavity of the renal pelvis, but sometimes a narrow band of closed ureter was visible between the two. The upper pool could be seen to fill either steadily or intermittently, and if there was a visible division between pool and pelvis, small urine spindles were seen to run from pelvis to pool at comparatively frequent intervals.

When filling had reached a certain stage a spindle of urine broke away from the lower end of the upper pool, driven downwards by a peristaltic wave which appeared to originate at this point, or else the entire pool moved downwards as a spindle.

This spindle then entered the lower pool. Often the peristaltic wave died out at this point, and as many as ten or a dozen waves might bring spindles from upper to lower pool without proceeding further. Finally one of the waves bringing a spindle from the upper pool would carry on over the lower pool, to produce a vigorous contraction of the lower portion of the ureter, and to drive a greater or lesser part of the contents of the lower pool through into the bladder.

Occasionally the wave responsible for this discharge of urine from the lower pool appeared to originate at the level of the pool itself, and not to result from a wave arriving from above.

Following a contraction of the lower part of the ureter, the lower pool lost perhaps half its contents, and it then refilled by stages as the cycle was repeated. Complete emptying did not occur unless a change was taking place from the pool pattern to the through spindle pattern.

With high rates of urine production, the spindles sent down from the upper pool were larger, and the peristaltic waves propelling them more vigorous. Under these circumstances, each wave travelled the length of the ureter, the spindle from the top entered the lower pool, the lower part of the ureter contracted, and an equal quantity of urine was forced into the bladder. The size of the lower pool thus remained unaltered by the passage of the wave.

When the lower end of the ureter contracted most of the lower pool was obliterated, the urine was forced into the extreme end of the organ, and part of it escaped into the bladder. With relaxation the remaining urine ran back into the lower pool position. Antiperistalsis was never observed, but this run-back, particularly when the residuum was large, looked confusingly like antiperistalsis, and even resembled reflux from the bladder.

Occasionally, particularly in the case of a third pool at the middle of the ureter, a peristaltic wave was seen to run across a pool, detaching a spindle from its lower end, but not obliterating the lumen in its passage.

In one dog bladder pressure was maintained at 20 cm water for several minutes. Through spindles of urine were none the less discharged into the bladder. Micturition then occurred with a further rise of bladder pressure, a pool formed at the lower end of the ureter, and discharge of urine from ureter to bladder continued during contraction of the bladder. A similar passage of urine into the bladder despite raised pressure was observed in several dogs and rabbits.

DISCUSSION

Lucas (1906) simultaneously recorded the pressure from two points on the ureters of dogs by inserting a cannula through the kidney substance into the renal pelvis and by introducing a T-tube through a slit made half-way down the organ. He recorded frequent, small waves from the pelvis; slow, larger waves from further down. This is the only previous work we know of in which an attempt has been made to measure ureteric pressures while allowing free drainage into the bladder. Later workers have recorded ureteric pressures by means of a catheter thrust up the lumen, the catheter being connected to a recording apparatus which presents a fixed and arbitrary resistance to the escape of urine (Trattner, 1932). It is evident that patterns recorded by such an arrangement can give little information about the normal activity of the ureter since the ureter above the catheter tip has the unnatural task of forcing urine down the catheter and through the machinery, whilst its natural task is to pass on urine to the piece of ureter next below it. Our method is an attempt to measure ureteric pressures while interfering as little as possible with normal function.

Fuchs (1936*a*, *b*) observed urine dyed with indigo carmine passing down the ureters of rabbits. When the bladder was allowed to drain through a catheter, he found urine to pass right through the ureter in spindles, but when the bladder was allowed to fill, or when the rate of urine production was high, he found that as much as the lower three-quarters of the ureter became filled with residual urine. There were sometimes two or three areas of residual urine, which he labelled 'cystoids'. The intervening closed portions of ureter he described as functional sphincters.

Fuchs referred to the formation of 'cystoids' as an 'opening reflex', and to their disappearance as a 'closing reflex'. He assumed that these 'reflexes' were controlled by afferents from the bladder, and that 'cystoid' formation enabled the ureter to force urine into the bladder against resistance. He assumed that pressure was higher in each succeeding 'cystoid', and that in the lowest 'cystoid' it was high enough to overcome bladder pressure, but stated that he was unable to confirm this idea by measurement since the insertion of a ureteric catheter would break down the system. He could not demonstrate the mechanism in dogs, but claimed to have observed it radiologically in humans.

Our observations upon the passage of dyed urine thus broadly confirm those of Fuchs, but differ in several important details. Fuchs does not report the progressive filling of a pool by spindles from above. The through spindle pattern was not, in our experience, limited to animals with freely draining bladders. Fuchs reports occasional reflux of urine into the ureter from the bladder in dogs, and occasional antiperistalsis in rabbits. These we never observed, and suspect that Fuchs was confused by the appearance of a run-back from the lowermost part of the ureter. We observed pooling in dogs and rats as well as in rabbits.

The pressure patterns obtained from dogs may be interpreted in terms of the observed movement of dyed urine. The pattern shown in Text-fig. 2, in which regular peristaltic waves in an upper section of the ureter accompany a rising basic pressure and a final large contraction lower down, is consistent with an upper pool feeding into a lower pool which finally empties part of its contents into the bladder.

The fact that an increased urine flow might convert a triple pressure trace showing a segmental pattern into one showing a through pattern is consistent with our observation that with diuresis, larger spindles ran from upper to lower pool, and each caused contraction of the lower part of the ureter, the peristaltic wave running straight through from top to bottom.

Triple traces showing through patterns in which flat base lines at zero pressures were recorded from each needle point between waves are consistent with the through passage of a spindle of urine from renal pelvis to bladder in an otherwise closed ureter.

Both pressure patterns and direct observation make it plain, therefore, that the ureter handles urine in two distinct fashions. Fuchs, as has been noted, believed that pool formation enabled the ureter to pump urine into the bladder against resistance, and it is true that either raising bladder pressure or increasing urine flow (both of which increase the work the ureter has to do) will bring about pool formation. Several questions, however, remain to be answered: what is the mechanism of pool formation; how does pool formation increase the power of the ureter as a pump; and under what physiological, as opposed to experimental, circumstances is there a call for this extra power?

It is unnecessary to postulate a reflex mechanism to explain lower pool formation. A peristaltic wave of given vigour will produce enough energy to force a given quantity of urine into the bladder against a given resistance. If either the quantity of urine, or the resistance to its onward passage become too great, the peristaltic contraction will succeed in ejecting none or only a part of the urine, and with the relaxation of the wave a quantity of urine will be left in the ureter. A succeeding wave, bringing another spindle, will meet muscle in the region of pooling which is already stretched by the residual urine, and it seems reasonable to suppose that the ureter, like the heart, will contract with greater vigour if its muscle is already stretched to some degree. Increasing the rate at which urine enters the ureter, or the resistance to its onward passage, will thus automatically bring about pooling and an increased vigour of peristaltic contraction until a new balance is struck between inflow and outflow.

Although raised bladder pressure or diuresis can thus be seen to give cause for the formation of a pool at the lower end of the ureter, they can scarcely account for the formation of upper and middle pools, or for the fact that peristaltic waves may carry urine as far as an upper, middle or lower pool without proceeding further. A possible explanation is that pool formation at the lower end of the ureter is accompanied by a general increase in the tone of the organ. We have no direct evidence of this, but an increase in tone would provide greater resistance to the discharge of urine from the upper half of the ureter and so encourage upper pool formation. Furthermore, tone in the ureter appears to increase from above downwards (Gould *et al.* 1955*a*), so that if propagation of a peristaltic wave is dependent upon distension of the lumen by the descending spindle of urine, it is possible that a spindle descending a ureter in a high state of tone will reach a point at which the force propelling it is insufficient to distend the lumen ahead, with the result that the wave dies out.

So much is speculation, but there is evidence that tone does play an important part when pools exist. Text-fig. 4 illustrates how raising bladder pressure may produce a rise in basic pressure at the lower end of the ureter while leaving the upper end either unaffected, or affected to a lesser degree. Such a tracing is consistent with the direct observation that a constriction may be maintained between an upper and a vigorously contracting lower pool, and with the idea that the closed section resists the backward flow of urine from the lower region of higher pressure in the periods between peristaltic contraction.

The nephrons are thus protected from the high basic pressures which may arise at the lower end of the ureter when the pool mechanism is in operation, and the protective factor must be the tone in the ureter separating areas of pooling.

The fact that basic pressure may rise and follow an identical pattern throughout the ureter if bladder pressure is raised during a period of very rapid urine secretion, is consistent with the idea that under such extreme conditions ureteric tone is incapable of maintaining a division between upper and lower ends.

Experiments on the isolated ureter of the water-buffalo (Gould *et al.* 1955*a*) suggest that in this animal tone is under the influence of both divisions of the autonomic nervous system, while rhythmical contractions are regulated largely by mechanical stimulation, specifically distension of the lumen. In intact animals, peristaltic activity runs parallel with the rate of urine production and can be induced or increased by distending the lumen with fluid. The measurement of tone in the intact animal presents difficulties which we have not yet overcome. Basic pressure is not an index of tone, for although it may be expected to vary with the tone of the organ, it also depends upon the rate of inflow and the resistance to outflow of urine. We have, therefore, not yet obtained any evidence concerning the influence of the nervous system on tone in the ureter of the intact animal. If it is accepted, however, that our findings for the isolated ureter of the water buffalo may be applied to the intact ureters of other animals, then it is likely that autonomic nerves regulate tone to suit the manner in which urine is being handled; and pressure measurements from the intact ureter suggest that an increase in tone is called for when a lower pool is pumping urine into the bladder against a high resistance. To this extent a reflex element may enter into pool formation. It would be reasonable to search for appropriate afferent fibres running from the bladder, and perhaps from the ureter itself.

The role of tone in preventing high pressures at the lower end of the ureter from being transmitted upwards gives point to the findings that in the isolated ureter tone increases from above downwards, and that autonomic drugs exert their maximum effect upon tone through the muscle of the lower end.

The ureter may continue to force urine into the bladder during micturition, but it is unlikely that an elaborate mechanism exists solely for ensuring the onward passage of urine during so brief and occasional an event. It is also difficult to accept the idea that a physiological mechanism exists specifically to cope with a high rate of urine production, since this is scarcely a normal state of affairs. Diuresis is common in man because he drinks quantities of fluid in excess of his requirements, water being a vehicle for several gratifying drugs and flavours. Other animals drink only what they need to maintain fluid balance, and do not fill their stomachs with water, merely to void it from the bladder within the hour. We have been able to show (Gould *et al.* 1955*b*) that bladder pressures vary greatly with posture, and that in man, intravesical pressures of 20–40 cm water are likely to exist throughout the working day. This, we believe, is why the mechanisms here described exist.

SUMMARY

1. Pressures were recorded simultaneously from three points on the ureters of dogs through hypodermic needles inserted into the lumen. In some dogs the issue of urine from the ureteric orifices was observed; in others bladder pressures were recorded together with pressures from two points on the ureter.

2. Observations were made upon the passage of urine, dyed with indigo carmine, along the ureters of dogs, rats and rabbits.

3. Both methods show that urine may either travel straight through the ureter in spindles propelled by peristaltic waves, or that pools of urine may form along the ureter, which receive urine from above and discharge it downwards after reaching a certain stage of filling. Pooling occurs with diuresis or raised bladder pressure.

4. We conclude that pool formation increases the vigour of peristaltic contractions and enables the ureter to do more work.

5. Pressures developed in pools at the lower end of the ureter are not transmitted to the upper end because of the tone of the intervening muscle.

6. We suggest that pool formation is dependent primarily upon mechanical factors, but that an accompanying increase in ureteric tone is reflex in origin and is due to stimulation of end organs in the bladder and perhaps in the ureter itself.

REFERENCES

Fuchs, F. (1936*a*). Über das reflexbedingte Verhalten der oberen Harnwege und seine Bedeutung für die Ausscheidungsurographie. *Z. urol. Chir.* **35**, 169–179.

Fuchs, F. (1936*b*). Theorie der Harnwegefunktion. *Z. urol. Chir.* **37**, 154–212.

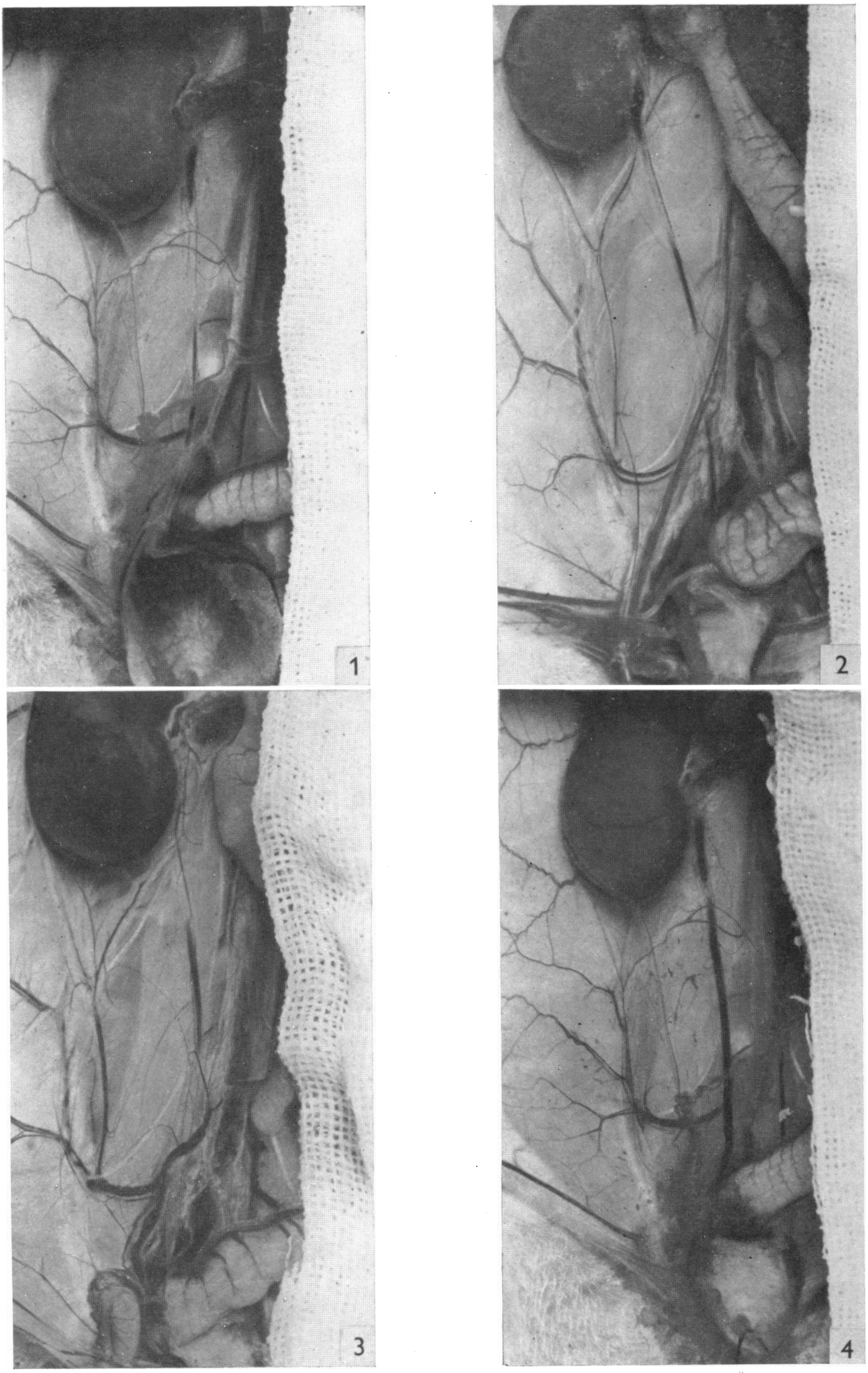
Gould, D. W., Hsieh, A. C. L. & Tinckler, L. F. (1955*a*). The behaviour of the isolated water-buffalo ureter. *J. Physiol.* **129**, 425–435.

Gould, D. W., Hsieh, A. C. L. & Tinckler, L. F. (1955*b*). The effect of posture on bladder pressure. *J. Physiol.* **129**, 448–453.

Lucas, D. R. (1906). Studies of the peristalsis of the ureter of dogs by the graphic method. *Amer. J. Physiol.* **17**, 392–407.

Satani, Y. (1919). Experimental studies of the ureter. *Amer. J. Physiol.* **49**, 474–495.

Trattner, H. R. (1932). Graphic registration of the function of the human ureter with the hydrophoragraph. *J. Urol.* **28**, 1–33.


1
2
3
4

EXPLANATION OF PLATE

Photographs of urine dyed with indigo carmine in the ureters of rabbits.

Fig. 1. Upper and lower pools exist. There was no movement in the ureter at the moment the picture was taken.

Fig. 2. A spindle of urine is travelling between an upper and a lower pool.

Fig. 3. A spindle of urine is travelling from renal pelvis to bladder straight down an otherwise empty ureter.

Fig. 4. The ureter is almost filled with urine but a small constriction remains between an upper pool and a very large lower pool.