SECRETION AS A FACTOR IN ELIMINATION BY THE BIRD'S KIDNEY. By E. B. MAYRS.

THE experiments on which the absorption theory of urinary secretion is based have been carried out for the most part on the amphibian and mammalian kidney. In the bird, however, absorption of fluid is largely relegated to the cloaca, and it is of interest to determine whether any modification of the renal process is associated with this peculiarity.

The kidney of the fowl is an elongated organ attached to the lower ribs; it is partially lobulated, and the ureter is formed by the junction of several tributaries embedded in the substance of the lobules. Microscopic examination, however, does not reveal any obvious structural departure from the mammalian type. The ureters are thick-walled ducts which open into the cloaca just above its sphincter. The normal urine is semi-solid in consistence, owing to a deposit of uric acid or urates; it contains a large amount of mucous material, and is usually mixed with fæces. But when urine is collected from the ureters without having had access to the cloaca it is found to be fluid, though often somewhat slimy in character. Excretion is generally rapid, and the liquid is sometimes quite transparent but frequently contains flakes of deposit. The flow of urine is presumably reduced by anæsthesia, with consequent increased absorption of water, and it is possible that under normal conditions uric acid is all in solution when it leaves the kidney. In any case, a great deal of water must be re-absorbed from the cloaca.

Minkowski(1) has obtained evidence that the uric acid of birds is formed for the most part from ammonium lactate, which is probably an end-derivative of protein catabolism. Milroy(2) found more recently that when acid is given to fowls the output of ammonia is increased at the expense of uric acid. In the metabolism of the bird, therefore, uric acid occupies a position analogous to that of urea in mammals, as a waste product derived chiefly from exogenous protein; and the need for continuous excretion of this substance is evident. The bird, however, is at a disadvantage, since its chief waste product is relatively insoluble; and the curious excretory arrangement which it has developed may have been designed to overcome this difficulty. Whether uric acid is eliminated by secretion or by glomerular filtration, it is unlikely to exist in the solid form in any cells of the kidney. Uric acid crystals have been observed in the tubule cells of the bird by v. Wittich(3). A post-mortem change in the reaction of the cell fluid might, however, have caused precipitation of uric acid, and Bial(4) could find no trace of solid urate in these cells. The bird cannot afford to lose even the minimum amount of water in which the daily output of uric acid could be dissolved, and hence some device must be adopted for re-absorption of water. If concentration of uric acid in the renal tubules were not limited, sufficient deposit might be formed there to interfere seriously with excretion. This is prevented by rapid diuresis, and loss of water is avoided by cloacal re-absorption. Occasionally fowls under ether or urethane anæsthesia exhibit complete anuria, and no diuretic will induce the kidneys to resume their function. This may indicate blocking of the renal tubules, resulting from slow passages of urine; the condition, however, has not been investigated.

The relative insolubility of uric acid, therefore, renders necessary continuous diuresis and re-absorption of water in the cloaca. It is not quite so clear whether any advantage would be gained by specific secretion of uric acid; but the possibility of this process in the bird deserves consideration. Sharpe(5) has found that adrenalin causes diuresis in fowls, and this is remarkable in view of its opposite effect in mammals. An increase in uric acid concentration may sometimes accompany the diuresis, and seems occasionally to occur with other diuretics also(6). This, too, is in contrast with mammalian excretion. The rapid elimination of fluid by the kidney, after injections of adrenalin, might be explained by supposing that local vaso-constriction is less complete or of shorter duration than that in other parts; the kidney would then obtain a good supply of blood at a higher pressure than usual. But a coincident increase in the concentration of uric acid seems to involve some secondary action on the renal cells; more probably an effect of the greater filtration than a direct action of the diuretic. Such evidence as is available, therefore, does not indicate much resemblance between the renal processes of birds and mammals.

Among methods employed to examine the action of the kidney in mammals two appear to be of special value, namely, comparison of the increase in concentration experienced by several waste products during their excretion; and observation of the changes produced in the urine when its outflow is resisted. Some experiments have now been carried out in which these tests were applied to the excretory function of birds.

Method. Cockerels were anæsthetised with ether or urethane, and the ureters were exposed by an abdominal incision. Cannulæ were introduced and the urine collected. Sometimes, when the fluid was not quite clear, intravenous injections of adrenalin were given, until the flow was sufficiently rapid to prevent the formation of deposit. This was not invariably done, however, and urines which contained a deposit of urates are marked with an asterisk. Blood was taken from the sciatic artery. Clotting is slow unless contamination with tissue juice has occurred; and as a rule no anti-coagulant was used, but the blood was collected in paraffined tubes, kept on ice, and centrifuged as soon as possible. The presence of oxalate or citrate is undesirable when certain colorimetric estimations are necessary.

The concentrations of uric acid and phosphate in the plasma and urine were compared; in later experiments creatine, creatinine, and chloride were examined in the same way, and occasionally urea and ammonia also. Removal of blood was postponed until sufficient urine had been obtained, in order that interference with excretion should be avoided. The collection of urine had, therefore, to be limited to a period during which the plasma remained fairly constant in composition. This condition appears to be fulfilled for intervals of at least 20 minutes. Thus, a particular sample of plasma contained 4·4 mgm. of uric acid and 3·4 mgm. of phosphate per 100 c.c. and a second sample from blood removed 20 minutes later contained 4·3 mgm. of uric acid and 3·0 mgm. of phosphate. Urine was generally collected for much shorter periods, however, since the amount required was often excreted in 1 to 5 minutes. Similar methods of analysis were employed for plasma and urine; the latter being diluted, when necessary, to about the same concentration as the former. Uric acid was estimated in the manner recently described by Benedict(7); phosphate by Bell and Doisy's method(8); creatine and creatinine by the method of Folin and Wu(9); chloride by Wetmore's application of Volhard's procedure(10); ammonia by the vacuum distillation process of Kruger, Reich and Schittenhelm(11); and urea in a similar manner, after hydrolysis with urease.

In three experiments the flow of urine from one kidney was resisted by using a long ureteral cannula which could be bent upwards to a vertical position. By this means pressures corresponding to about 15–25 mm. of mercury were applied, and the concentrations of uric acid and phosphate found in the urine were compared with those of normal urine excreted simultaneously by the other kidney.

In several of the earlier experiments samples of plasma were ultrafiltered, in order to test the diffusibility of the uric acid and phosphate which they contained; for if part were attached to colloids the failure to recognise this would invalidate comparisons of their $\frac{\text{urine}}{\text{plasma}}$ ratios, since only the diffusible portions could be excreted. A protein-free fluid was obtained by filtration through small collodion tubes at a pressure of about 10 lbs. per sq. inch[1]. The first portion of the filtrate was rejected in order to avoid dilution. Examples are given in Table I of the concentrations of uric acid and phosphate in several samples of plasma before and after filtration.

TABLE I. *Mgm. per* 100 *c.c.*

Uric acid		Phosphate (*P*)	
Plasma	Ultra-filtrate	Plasma	Ultra-filtrate
3·4	3·3	2·4	2·1
4·6	4·9	8·1	5·4
6·7	6·8	1·8	1·5
16·1	16·1	5·6	5·4

These results show that the uric acid of fowls' plasma, or that part of it which can be estimated in a tungstic acid filtrate, is able to pass through a collodion membrane. Most of the phosphate can pass through also; a small proportion may be adsorbed on the membrane, for even dilute protein-free phosphate solutions of known strength appear to become weaker during filtration. There is, of course, no proof in either case that part is not attached to colloids removed by precipitation or filtration; but the precipitation methods employed evidently do not interfere with satisfactory measurement of the diffusible portions, and these alone are of importance in connection with excretion[2].

The figures given here and in other parts of this paper indicate that the plasma content both of uric acid and phosphate is subject to considerable variation. Folin and Denis(12) found 4·8 mgm. of uric acid in 100 c.c. of bird's blood, and Robertson(6), using the same method, found 5·15 and 6·16 mgm. Later, Folin and Wu(9) obtained by their more recent procedure amounts varying from 2·5 to 3·8 mgm. per 100 c.c. Most of my own results fall within the somewhat wide range of those reported by other observers, but there is no doubt that, under anæsthesia

[1] I am indebted to Dr Dale for suggesting the use of the centrifuge to remove air-bubbles from tubes filled with collodion; and also for pointing out that when the excess of collodion had been poured off 50 p.c. alcohol could be introduced, without preliminary drying of the film. Suitable thimbles were made by this method in about 10 minutes.

[2] White (*Amer. Journ. Physiol.* 65. p. 200, 1923) assumes that because the phosphate of ox plasma is diffusible this is also true of dogs; and the discordant results which he obtains when comparing normal phosphate excretion with the excretion of injected phosphate may be due to inclusion, in the former case, of phosphate attached to colloids.

at any rate, the quantity of uric acid present may occasionally be much greater. The highest concentrations observed exceeded 16 mgm. per 100 c.c. of plasma.

For the purpose of this investigation, however, the absolute quantities of uric acid and phosphate are not of importance, since only their $\frac{\text{urine}}{\text{plasma}}$ ratios are required. These were generally obtained by direct colorimetric comparison of tungstic acid filtrates from plasma with diluted urine to which the same reagents had been added. The actual amounts present were subsequently determined by means of standard solutions. On one occasion 20 c.c. per kilo of 10 p.c. sodium sulphate were injected intravenously, and the concentration of this substance by the kidney was compared with that of uric acid. The second table shows the results of this experiment, as well as of those dealing with uric acid and phosphate.

TABLE II.

No.	Vol. of urine c.c. per min.	Uric acid in plasma mgm. per 100 c.c.	Uric acid in urine mgm. per 100 c.c.	$\frac{\text{Urine uric acid}}{\text{Plasma uric acid}}$	Phosphate in plasma mgm. P per 100 c.c.	Phosphate in urine mgm. P per 100 c.c.	$\frac{\text{Urine phosphate}}{\text{Plasma phosphate}}$	Concentration of uric acid by kidney Phosphate = 1
1	1·70	4·4	67·4	15·3	3·4	9·0	2·6	5·9
2	·44*	4·3	269·8	62·7	3·2	36·5	11·4	5·5
3	·58	3·4	53·9	15·9	2·4	6·9	2·9	5·5
4	·48*	16·1	327·9	20·4	5·6	21·2	3·8	5·4
					Sulphate in plasma gm. Na_2SO_4 per 100 c.c.	Sulphate in urine gm. Na_2SO_4 per 100 c.c.	$\frac{\text{Urine sulphate}}{\text{Plasma sulphate}}$	Concentration of uric acid by kidney Sulphate = 1
5	·30	6·4	84·6	13·2	·62	1·24	2·0	6·6

It will be seen in Table II that the $\frac{\text{urine}}{\text{plasma}}$ concentration ratio of uric acid is more than five times as high as that of phosphate, and more than six times as high as that of sulphate. If this means that uric acid is secreted, the constancy of these relations suggests that phosphate and sulphate are concentrated mainly by re-absorption of water. The possibility of secretion of phosphate will, however, be considered later. Experiments in which the urine contained a deposit can be criticised on the ground that solid material may accumulate for some time in the tubules and leave the kidney at intervals, thus producing a sudden increase in the uric acid content of the urine and rendering it useless as a measure of the concentrating power of the kidney. If this were so, the relation between the concentration ratios of uric acid and phosphate would not be uniform;

but it is found that this relation remains the same whether deposit is present or not, so long, at least, as the flow of urine is not less rapid than those recorded. In other words, when the urine contains solid uric acid there is an equivalent rise in its phosphate content. Hence, there is reason to believe that no accumulation of uric acid in the tubules has occurred.

The results obtained by applying a similar method of investigation to other constituents of the plasma and urine are grouped together in Table III.

TABLE III.

		Plasma concentrations mgm. per 100 c.c.					Urine concentrations mgm. per 100 c.c.					Urine/Plasma				
No.	Vol. of urine c.c. per min.	Uric acid	Phosphate (P)	Creatine	Creatinine	Chloride (NaCl)	Uric acid	Phosphate (P)	Creatine	Creatinine	Chloride (NaCl)	Uric acid	Phosphate	Creatine	Creatinine	Chloride
1	·55	8·6	—	6·4	1·5	—	124·8	—	17·4	4·1	—	14·5	—	2·7	2·7	—
2	·38	6·1	1·2	5·1	1·3	670·0	197·9	Nil	14·1	3·9	240·0	32·4	—	2·8	3·0	·36
3	·68*	—	4·9	4·0	1·3	690·0	—	36·5	22·5	5·4	20·0	—	7·4	5·6	4·2	·03

Urea and ammonia are not included in this table, because the method of estimation employed was not found sufficiently delicate to give very accurate results with the quantities of plasma available. The total urea and ammonia nitrogen of the plasma does not appear to exceed 0·7 mgm. per 100 c.c. In urine collected from the ureters as much as 28 mgm. per 100 c.c. may be present; in one sample four-fifths of the total was in the form of ammonia, but there is no evidence that this is always the case. At any rate urea and ammonia are only excreted in small amount by the bird, and are of relatively little importance. Table III shows that uric acid is the principal waste product in the urine. It is well known that creatine is largely excreted unchanged; the quantitative relation between this substance and creatinine is indicated in the table. Chloride is at a lower concentration in the urine than in the plasma, and the very limited excretion of chloride in Exp. 3 suggests that it may sometimes be absent from concentrated urines. Phosphates also may apparently be retained, for none could be detected in the urine of Exp. 2, when the plasma content was only 1·2 mgm. per 100 c.c.

It is probable that this investigation has included all the important waste products excreted by the kidney of the bird, and the fact of most interest is that uric acid, during elimination, undergoes a much greater increase in concentration than any other substance examined. Urea and ammonia may perhaps be exceptions; the results obtained in connection with excretion of nitrogen in these forms indicate that a

$\frac{\text{urine}}{\text{plasma}}$ ratio of 40 is possible. But in view of the statement by Davy (13) that nearly all the ammonia of birds' urine is in combination with uric acid, this observation is not of much value in deciding the mechanism of excretion; for the substances to be compared must obviously be independent of one another. Creatine and creatinine seem to be slightly inferior to phosphate as regards the efficiency of their elimination. Chloride is not concentrated at all and is, therefore, of no interest for comparison.

Uric acid, then, experiences a greater increase in concentration than any other substance which passes from the plasma into the urine. This can only be explained by admitting secretion of uric acid, or by postulating extensive re-absorption of everything else. The secretion theory is, of course, much more probable, but these experiments furnish no evidence as to whether anything except uric acid is secreted. In any case, uric acid is in a class by itself; in the bird there is no group of substances which conforms to Cushny's definition of no-threshold bodies.

The figures given in Table III are of interest from another aspect. When the concentrations of the plasma and urine are calculated from a physical standpoint, it is clear that the fluid which leaves the kidney of the bird must be hypotonic. The total force exerted by the kidney in overcoming osmotic tension is, therefore, on the whole applied in a direction opposite to that which ordinarily characterises mammalian excretion. Chloride is, of course, the deciding factor, and since this substance may be almost absent from the urine, although it probably passes through Bowman's capsule at plasma concentration, there is good reason to suppose that it is re-absorbed in the renal tubules. Hence it seems to be in re-absorption that the anomaly occurs; the mammal generally increases the osmotic pressure of the tubule fluid by absorption (since relatively little urea is absorbed), but the bird appears to reduce it by the same process. The hypotonicity is of importance in the analogy to other secretions which it suggests.

Uric acid is excreted so efficiently that the amount lost by the plasma in the renal circulation is probably considerable. Water is eliminated also, and it is evident that an observed decrease in uric acid concentration cannot be so great as to represent the true loss of uric acid. However, an attempt was made to obtain blood from the renal veins for comparison with arterial blood. This is difficult owing to the impossibility of ligaturing other veins which communicate with the renal. The hypogastric vein lies on the anterior surface of the kidney, and is closely applied to this surface throughout almost the entire length of the organ;

the renal blood is carried to this vein by vessels which pierce its posterior wall as soon as they leave the kidney. The femoral vein is also a tributary of the hypogastric. Ultimately the renal circulation was isolated by tying the femoral vein and inserting a cannula into the proximal portion; then enlarging the opening through which this vessel enters the abdomen and applying digital pressure to the hypogastric vein at the upper and lower poles of the kidney, with two fingers introduced through the opening. As soon as the upper point was compressed, renal venous blood was allowed to flow from the cannula, and was collected for a short period. The circulation through the kidney is evidently slower than in mammals. About 5 c.c. of venous blood were obtained in 2 or 3 minutes. Arterial blood taken from the sciatic artery in the usual way is the same as that which supplies the kidney. The arterial sample of plasma collected was found to contain 13·2 mgm. of uric acid per 100 c.c. and the venous sample 10·3 mgm. Hence, there was a loss of 3 mgm. per 100 c.c. without allowing for concentration of the blood by removal of water; or nearly a quarter of the uric acid brought to the kidney. When the concentration factor is considered the efficiency of excretion is still more evident.

The remaining experiments deal with the effect of resisting the outflow of urine; the method employed was quite simple, and has already been described. At first the pressure was applied to one ureter only, and the urine compared with that excreted normally by the other kidney. But with no interference at all the minute volumes and concentrations of the urines from the two sides may be quite different, and the urine from either kidney is subject to rapid variations in character. In a later experiment, therefore, each kidney in turn was made to excrete against resistance, and comparison was thus possible with the fluid excreted before and after the period of pressure, as well as with the normal output of the unresisted kidney during this period. The results are given in Table IV.

TABLE IV.

	Vol. of urine c.c. per min.		Uric acid mgm. per 100 c.c.		Phosphate mgm. *P* per 100 c.c.	
No.	Normal	Pressure	Normal	Pressure	Normal	Pressure
1	**·48***	·08	**327·9**	269·7	**21·2**	13·2
2 (*a*)	**·62** ·70	—	**106·7** 82·0	—	**14·8** 14·6	—
(*b*)	**·18***	·03*	**218·4**	229·9	**28·4**	35·3
(*c*)	·19*	—	565·6	—	15·7	—
3 (*a*)	**·53*** ·15	—	**253·2** 178·9	—	**17·0** 10·6	—
(*b*)	·40	**·10***	207·5	**361·4**	9·8	**32·3**
(*c*)	**·51**	—	**346·8**	—	**18·8**	—
(*d*)	**·58**	·08	**175·5**	232·6	**11·5**	11·3
(*e*)	1·17	—	195·7	—	6·9	—

In Table IV the figures from left to right represent simultaneous rates of flow and concentrations. The column in which the figures are placed indicates whether or not pressure was being applied during the period in which the urine was collected. Throughout the table figures referring to the right kidney are in heavy type, and, as before, an asterisk denotes the presence of deposit, which was included in the estimation of uric acid.

In observing the effects of resistance, the urines from the right and left ureters cannot readily be compared with one another, since the volumes and concentrations may differ greatly before either kidney is excreting against pressure. It is interesting to notice in this connection that a slow rate of flow is not necessarily accompanied by a high concentration of uric acid and phosphate; for the urine from the kidney which has been excreting more rapidly may contain a greater percentage of these substances. Resistance, however, seems invariably to reduce the outflow of urine, not only below the level which existed before pressure was applied, but also below the simultaneous rate of flow from the other kidney. The urine is more concentrated than it was before, but not necessarily more concentrated than that from the other kidney which is excreting normally. The increase in concentration is not invariably greater for one substance than for the other, as would be the case if one were a no-threshold and the other a threshold body. But when the resistance is removed and a greater outflow of urine begins, the concentration of phosphate is observed to fall to a half or two-thirds of its previous value, while uric acid does not undergo so much dilution. In Exp. 2, at this stage, instead of a reduction in uric acid its concentration was more than doubled. In this case, however, solid uric acid had probably accumulated in the renal tubules, and was forced out when the pressure was removed. Such an occurrence is unlikely in the case of phosphate; it is apparently the result of re-absorption of water, and this process is not sufficiently complete to throw the phosphate out of solution. In Exp. 3, when the outflow was no longer resisted, the urines excreted were fairly clear. They did not contain quite so much uric acid as had been present when the kidneys were working against pressure, but the decrease was not comparable to the corresponding reduction in phosphate. Thus the $\frac{\text{uric acid}}{\text{phosphate}}$ ratio in urine from the right side rose from 11·2 to 18·5 and in urine from the left side this ratio increased from 20·5 to 28·4. This may indicate that uric acid (probably in solution) is normally stored in the renal cells, and that more accumulation occurs when the flow of glomerular filtrate is reduced. When active filtration is resumed excess of uric acid may be secreted, though its concentration may be lowered by the greater amount of filtrate. The comparative method can give no evidence of a phosphate storage, but the fact that this substance may, like uric acid, exist at higher concentration in normal urine from one kidney than in a smaller volume of urine simultaneously excreted by the other against resistance (see Exp. 1) suggests that phosphate also is secreted to some extent.

Summary and Remarks.

(1) Uric acid undergoes a greater increase in concentration than the other constituents of the urine. It can scarcely be held that all other waste products are re-absorbed from the glomerular filtrate; to the extent of at least four-fifths in most cases.

(2) The concentration of uric acid has no definite inverse relation with diuresis; a rapid flow of urine does not necessarily result in a low concentration of this substance. It might be argued that some may be re-absorbed during slow excretion, but this is unlikely in view of the fact that uric acid is better concentrated than anything else.

(3) The urine excreted by the two kidneys may differ in amount and concentration. The quantity possibly depends on the number of glomeruli which happen to be in action; but the percentage of uric acid is often greater in the larger volume of urine. Local changes in cell activity evidently occur, which are independent of the composition of the blood; otherwise the fluids from the two ureters would be more similar in character. This seems to indicate the existence of secreting cells in the kidney.

(4) While the concentration of uric acid may be increased by resisting the outflow from one ureter (and thus promoting re-absorption of water), the fluid obtained may not even then contain more of this substance than the urine flowing unresisted from the other kidney. Experimental interference of this sort does not appear to have much real effect, and, as Cushny has pointed out, secretion should be independent of small changes in pressure.

(5) Phosphate behaves in a somewhat similar manner in conditions of diuresis and resistance. Hence, phosphate also may be secreted; but secretion in this case is clearly of much less importance, since the increase in concentration is not nearly so great. The ratios of phosphate to uric acid are usually different in simultaneous samples of urine from the two kidneys, although the same blood supplies both organs. Thus the local renal activity may vary independently for these two substances,

and this may indicate that different groups of cells are concerned in their secretion.

(6) The urine is hypotonic, and in this respect resembles the product of a secreting gland.

These considerations leave little doubt that the kidney of the bird can secrete. Re-absorption is possible also, although the use of the cloaca for this purpose renders the process less necessary than in the mammalian kidney. The effect of resistance in causing increased concentration of the urine seems to indicate that water can be absorbed from the renal tubules. Chloride and occasionally phosphate may be re-absorbed, for the urine may contain less than the plasma. In Exp. 5, Table II, there was 1·24 p.c. of sulphate in the urine. If any re-absorption of water occurred in this case (and it probably always occurs to some extent), the last stage of concentration was almost certainly attained by this process. Hence, the tubule cells can remove water against great osmotic resistance when they are called upon to do so.

Since birds and mammals have a common ancestry, it seems reasonable, at first sight, to assume that if the kidney of the bird can secrete so also can the mammalian kidney; and to ignore the absence of satisfactory proof of secretion in the mammal. But there are serious objections to the analogy. None of the evidence of secretion obtained in this investigation is applicable to mammals, in which nearly all the observations described have already been made with opposite results. In the mammal several waste products (no-threshold bodies) experience an almost equal increase in concentration while they are being excreted, and hence are probably concentrated by re-absorption of water. The urine from the two kidneys is generally similar in amount, and when some difference does occur in the rate of excretion the concentration of no-threshold bodies is either the same on both sides or somewhat greater in the smaller volume. Evidently the rate at which glomerular filtrate flows through individual tubules is usually about the same in both kidneys, and the quantity of urine is largely determined by the number of excreting units in action. Roughly the same proportion of fluid is therefore re-absorbed in both cases. If secretion were possible, local variations in cell activity would probably occur, and produce results similar to those described in birds. Diuresis reduces the concentration of the urine in mammals, and a slow outflow causes increased concentration. When one kidney is excreting against pressure its urine is more concentrated than that of the other, as regards no-threshold constituents at any rate[1]. This is to

[1] The discrepancies in the results obtained by different observers as regards the effects

be expected in the absence of secretion, since more time is allowed for the re-absorption of water. The urine of mammals is nearly always hypertonic; for even when a considerable quantity of chloride is being retained the concentration of urea and no-threshold bodies ensures hypertonicity. In this characteristic the urine differs from most secretions.

In conclusion, then, it is clear that the bird has developed a distinctive excretory mechanism, in which selective re-absorption by the kidney plays only a minor part. No great quantity is found in the urine of any substance which can offer osmotic resistance to concentration. A relatively insoluble waste product is excreted in large amount, and the process involved would not necessarily be suitable for the excretion of soluble substances at a high concentration, such as the kidney of mammals can produce.

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of resistance on the volume of urine appear to be explained by the experiments of Lucas, *Amer. Journ. Physiol.* 22. p. 245, 1908, who found that in the dog moderate resistances do not always increase the pressure in the renal pelvis. In such cases the volume of urine may be greater owing to a nerve reflex from the ureter; but it is probable that when the pressure is actually raised in the pelvis, the kidney, if normal, always excretes less urine, and the concentration of no-threshold bodies is necessarily increased.