THE SUPRARENAL BODIES AND DIURESIS.

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WHILST carrying out perfusion experiments on the kidneys of cats I was struck by the different effects produced by perfusing (*a*) directly through the renal arteries and (*b*) through the aorta.

The kidneys were perfused *in situ*, the intestines only (together with the spleen) having been removed between ligatures.

(*a*) In the first series of experiments the afferent cannulæ were inserted in the renal arteries: the perfusion fluid escaped from cannulæ inserted in the inferior vena cava, or in the renal veins if it was desired to record the circulation through the two kidneys separately: whilst the urine was collected by means of the bladder-cannula which I have described elsewhere[1].

(*b*) In the second series of experiments the afferent cannula was tied into the thoracic aorta immediately above the diaphragm: all vessels that could be seen coming from the aorta were ligatured except the renal arteries, and the aorta was ligatured below the renal arteries. The perfusion fluid issuing from the kidneys and the urine was collected as in the first series.

The perfusions were carried out at a constant pressure of 80–90 mm. Hg. The perfusion fluid was kept at a constant temperature by means of a water-bath, the temperature of the fluid as it entered the vessels being about 36° C. The urine was collected every ten minutes and accurately weighed in a tared flask.

During the first 30–45 minutes or more of each experiment oxygenated Ringer's solution was perfused. The experiments in which the perfusion fluid flowed directly into the renal arteries showed invariably a progressive rise in the amount of urine, usually (but not always) accompanied by a progressive increase in the rate of flow of the perfusion fluid (Fig. 1). Those experiments in which the perfusion was made into the aorta, on the other hand, showed a progressive fall in the

[1] Cow. This *Journal*, XLVIII. p. 1. 1914.

amount of urine, accompanied by a progressive fall in the rate of flow of the perfusion fluid (Fig. 2). Sometimes when the perfusion was continued for a longer period (4–5 hours) the increase or diminution in the flow of urine was not constant, though it always was so for at least two hours after the commencement of the perfusion. This agrees in the main with Sollman's results in perfusing the isolated kidney[1].

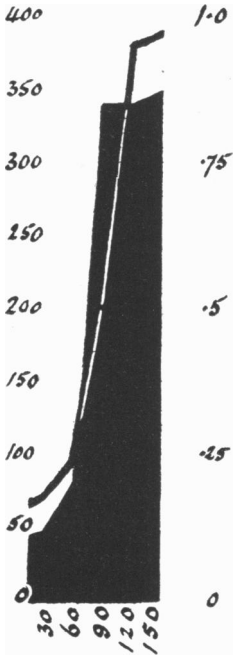

Fig. 1.

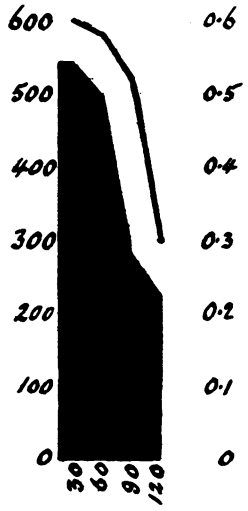

Fig. 2.

Fig. 1. Rate of flow of perfusion fluid and of urine. Kidneys perfused with Ringer's solution directly into the renal arteries. The single line = perfusion fluid. The shaded curve = urine flow. Ordinate = c.c. of perfusion fluid and c.c. of urine. Abscissa = time in minutes.

Fig. 2. Rate of flow of perfusion fluid and of urine. Kidneys perfused with Ringer's solution through the aorta. The single line = perfusion fluid. The shaded curve = urine flow. Ordinate = c.c. of perfusion fluid and c.c. of urine. Abscissa = time in minutes.

After excluding all possible sources of difference in the conditions of the experiments, the only feasible explanation appeared to be that in those experiments in which the perfusions were made into the aorta there was a circulation through the suprarenal bodies, though under

[1] Sollman. *Amer. Journ. of Physiol.* XIII. p. 241. 1905.

the conditions in which the perfusions were carried out it was not easy to understand in what way fluid perfused through the suprarenal bodies could reach the fluid flowing through the kidney vessels.

An experiment was then performed as follows:—a cat, anæsthetized first with A.C.E. mixture and then with urethane, was eviscerated (stomach, intestines and spleen): a cannula connected with the perfusion

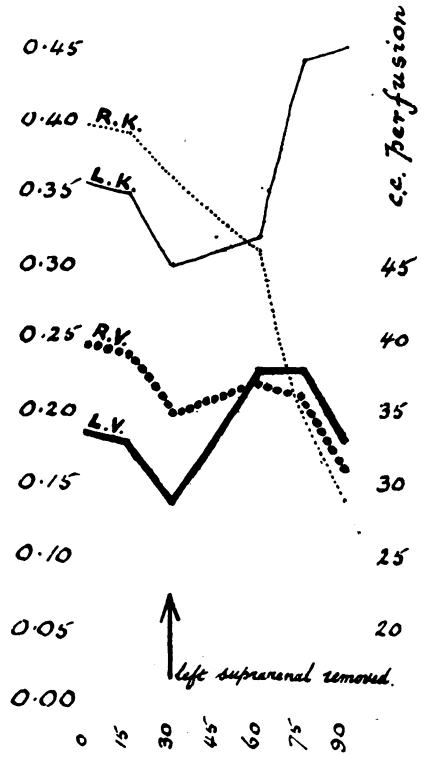

Fig. 3. Rate of flow from renal veins and from ureters. Kidneys perfused with Ringer's solution through the aorta. Ordinate = c.c. of perfusion fluid and c.c. of urine. Abscissa = time in minutes. ····· = flow from right ureter (*R.K.*). —— = flow from left ureter (*L.K.*). ●●●●● = flow from right renal vein (*R.V.*) ▬▬ = flow from left renal vein (*L.V.*) At the point indicated the left suprarenal was ligatured off and removed.

fluid reservoir was tied into the aorta just above the diaphragm: cannulæ were tied into the two renal veins: the aorta was ligatured below the renal arteries and all branches of the aorta that could be seen between the afferent cannula and the renal arteries were ligatured. The ureters were catheterized with capillary glass tubes introduced by means of horsehair probes. The kidneys were then perfused with Ringer's

solution at constant temperature (about 36° C.) and pressure (80 mm. Hg.). The perfusion fluid and urine were collected separately from each kidney and accurately measured every 15 minutes. After perfusing for 30 minutes the left suprarenal body was quickly ligatured off and extirpated. The result of this experiment is shown in graphic form in Fig. 3. During the first 30 minutes the flow of urine from the two kidneys and the flow of perfusion fluid followed parallel curves. After the removal of the left suprarenal body the flow of urine from the right kidney continued to fall, whilst that from the left kidney began to rise, whereas before the extirpation of the left suprarenal body it was falling in company with that on the right side. After the removal of the left suprarenal body the flow of perfusion fluid from the renal veins rose on both sides, the rise on the left side being much more marked than that on the right side. This experiment was repeated on three other cats always with the same result.

It is known that the vessels in the neighbourhood of the kidneys anastomose with vessels connected with adjacent parts, thus Tuffier[1] and Quenu and Lejars[2] describe anastomoses between the vessels of the kidney, suprarenal and large intestine.

The kidneys and suprarenal bodies of three cats were then injected with a gelatine-carmine mass after killing the animals with coal-gas, in order to dilate all the vessels. The first animal was injected through the aorta: no vessels were tied, so that the injection mass was free to pass into any vessels below the diaphragm. The second animal was injected into the thoracic aorta: the intercostal arteries and cœliac axis were tied, as also were the main suprarenal veins at their entrance into the vena cava: the aorta was ligatured above the renal arteries and the vessels in the hilum of the kidney were cut through. In this case the injection mass was free to pass into any vessels leading to the suprarenal bodies from either the aorta or the phrenic arteries: the injection mass could not reach the kidneys excepting through vessels entering them through the capsule. The third animal was injected into the renal artery direct, the cannula being pushed as far into the pelvis of the kidney as possible. A ligature was tied round all the tissues between the renal artery and the suprarenal body, in order to prevent the injection mass reaching the suprarenal body through any branches of the renal artery supplying the suprarenal body. The renal vein was cut and as soon as the injection mass issued therefrom it was tied.

[1] Tuffier. *Revue de Chirurgie*, p. 390. 1890.

[2] Quenu and Lejars. *Etude sur le systeme circulatoire*, Paris, 1894.

The injection was then continued. After injection the tissues were hardened *in situ* before removal for dissection.

The first injected specimen showed a fine rete of vessels formed from branches of the aorta leading to the suprarenal bodies. The main drainage of the suprarenal bodies was into the large veins which cross them, one on each side, immediately before joining the inferior vena

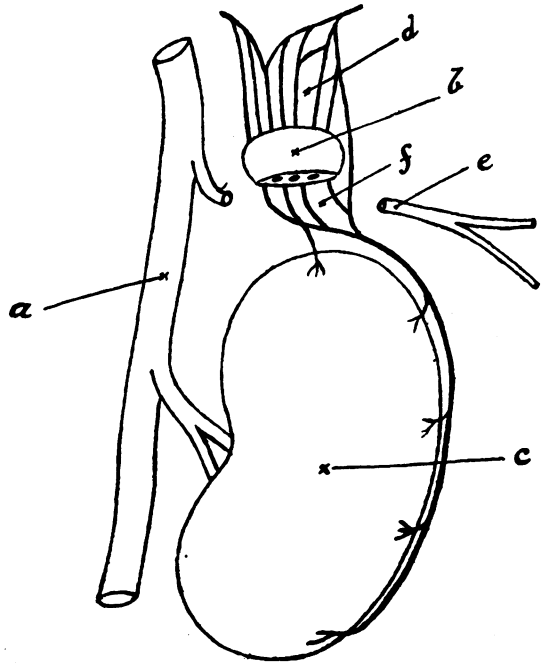

Fig. 4. Diagrammatic representation of vascular arrangement between suprarenal body and kidney. The suprarenal body has been cut away from the large vein which crosses it—part also of this vein has been removed in order to show the fine rete of vessels beneath. *a*, inferior vena cava. *b*, left suprarenal body. *c*, left kidney. *d*, rete of vessels from aorta and branches supplying suprarenal body. *e*, vein which receives the bulk of venous blood from suprarenal body. This has been dissected away from the suprarenal body, with which it is normally in close contact. Part too of this vessel has been removed in order to show: *f*, rete of vessels between suprarenal body and kidney. These vessels are for the most part embedded in the peri-renal fat and supply branches which dip beneath the capsule of the kidney.

cava. Behind these veins and embedded in the peri-renal fat was another fine rete of vessels coming from the suprarenal bodies. This rete joined up into a small vessel which supplied branches entering the kidney through the capsule around the convex border of the kidney. Accompanying some of these vessels entering the kidney were other

vessels (obviously veins) which on leaving the kidney joined up into a vessel which emptied itself into the main suprarenal vein. The general arrangement of these vessels is shown in Fig. 4.

Similar vascular connections were found in the other two specimens. In the case of the second specimen the kidney was cut open longitudinally and it was found that the injection mass had entered the kidney and that cuneiform areas of the kidney were coloured. These areas had their bases on the renal capsule in positions which corresponded with the entrance of the vessels through the capsule, as described above. The apices of these injected areas extended into the medulla of the kidney, converging on the calyces (Fig. 5).

In the third specimen the suprarenal bodies were isolated from the surrounding tissues and appeared to be uninjected: on cutting them open longitudinally, however, it was found that the cortex was uninjected whilst the medulla was full of injection mass. The contrast between the pale cortex and the deeply injected medulla was extremely marked. With the exception of a portion of the cortex at the hilum, where there were many injected vessels, only a few minute injected vessels were seen crossing the cortex to reach the medulla (Fig. 6).

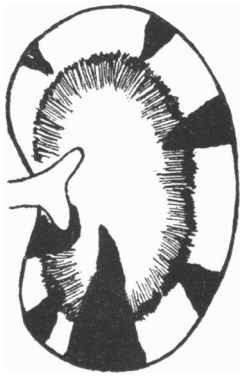

Fig. 5.

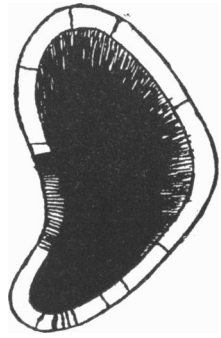

Fig. 6.

Fig. 5. Diagrammatic representation of appearance presented by section of kidney which was injected through the reno-suprarenal vessels. The darkly shaded parts indicate the parts of the kidney showing injection.

Fig. 6. Diagrammatic view of section through suprarenal body which was injected with gelatine-carmine mass through the reno-suprarenal vessels. The shaded parts indicate those parts injected.

It appeared, then, that there exists at any rate a possible channel through which the products of the suprarenal bodies can reach the kidneys directly and without either dilution or oxidation in the general

circulation. In order to clinch the matter a cat under urethane was bled from (*a*) the carotid artery, (*b*) the femoral artery, (*c*) the renal vein and (*d*) the stripped off kidney capsule, whilst the sciatic nerve was being stimulated[1]. The main suprarenal vein in this animal had been ligatured close to its junction with the vena cava, in order that the products of the suprarenal bodies might not be poured out into the general circulation. These samples of blood were whipped and filtered through glass-wool and diluted with an equal volume of Tyrode solution. Portions were then injected intravenously into a cat under urethane, and though the blood from the stripped kidney capsule appeared to have a more pronounced pressor action on the blood-pressure than the other samples of blood the difference was too small to be relied on. The more sensitive method described by Dale was then tried. The uterus of a guinea-pig was removed and suspended in a bath of warm

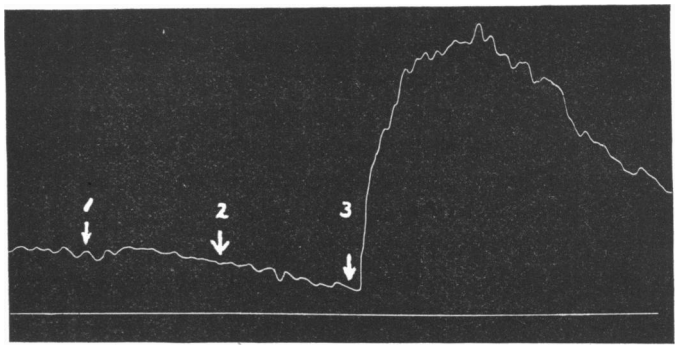

Fig. 7. Pregnant uterus of guinea-pig in bath of Tyrode solution at 36° C. At 1, 1 c.c. of blood from the carotid artery; at 2, 1 c.c. of blood from the renal vein; and at 3, 1 c.c. of blood from the stripped kidney capsule of a cat were added to the solution. Upstroke = contraction.

(36° C.) Tyrode solution, so that it pulled on a counterbalanced lever. On adding small quantities of the different samples of blood to the Tyrode bath it was found that, whereas the blood from the femoral and carotid arteries and from the renal vein produced no effect on the uterine contractions, the sample collected from the stripped off kidney capsule had a strong pressor action, identical indeed with that of adrenalin, as was shown afterwards on the same isolated organ. These results were confirmed by repetition of the experiment on other animals

[1] It has been shown by Elliott (This *Journ.* XLIV. 374. 1912) that stimulation of the sciatic nerve produces a reflex exhaustion of the adrenalin content of the suprarenal bodies.

and by repeated applications of the various samples of blood in each case (Fig. 7). No appreciable diminution in the pressor activity of the renal capsule blood was found even when it was collected from an animal in which the main suprarenal vein had not been tied.

It is obvious, then, that the products of the suprarenal body not only can but under certain conditions do actually enter the kidney directly without previous dilution or oxidation in the general circulation.

It has been shown by Asher and Pearce[1] that stimulation of the splanchnic nerve causes a diminution in the flow of urine, whilst, with the splanchnics cut through, stimulation of the vagus is followed by an increase in the amount of urine. These authors suggest, though this is denied by others, that the vagus and splanchnics are direct secretory nerves to the kidney.

Elliott[2] shows that fright or excitation of afferent nerves causes a reflex exhaustion of the adrenalin content of the suprarenal bodies, and that the efferent path of this reflex is by the splanchnics.

If it can be demonstrated, then, that adrenalin has the same action on the flow of urine as has stimulation of the splanchnics, there is at hand an obvious explanation of the results of Asher and Pearce without introducing the hypothesis that the kidney has a direct secretory innervation: namely that stimulation of the splanchnic nerves produces an outflow of adrenalin from the suprarenal bodies and that some at any rate of this adrenalin finds its way directly to the kidney, producing a diminution in the flow of urine.

That this is the case is shown by the following experiment: a cat anæsthetized with urethane was eviscerated (stomach, intestines and spleen). The right ureter was tied, the right suprarenal body was extirpated and the left suprarenal vein was ligatured close to the vena cava. Thus no suprarenal products could reach the general circulation except after passage through the left kidney. The urine from the left kidney was collected and a drop record taken. After leaving the animal to recover from any shock due to the operation the sciatic nerve was stimulated. Before the stimulation the urine was flowing at the rate of 4·5 drops per min.: during the stimulation the flow rose for a short period to six drops per min., then rapidly fell to about two drops per min. and remained at or about this level for a considerable time. Later, when the rate of flow had recovered an intravenous injection of

[1] Asher and Pearce. *Ztschr. f. Biol.* LXIII. p. 83. 1913.
[2] Elliott. *Loc. cit.*

adrenalin was given at a time when rather less than four drops of urine were being registered per min. The urine flow rose at once to 7·5 drops per min.: this rise was but momentary and was followed by a fall to about one drop per min., which rate was maintained for some time. These two curves are shown in Fig. 8. On repeating this experiment precisely similar results were obtained.

A few experiments were then carried out with the idea of showing that possibly pilocarpine might produce an increased flow of urine when the suprarenal bodies were intact, and that it might be without this effect after extirpation of the suprarenals. Though seven experiments were performed the results were not conclusive; though on one occasion an injection of pilocarpine produced an increase in the flow of urine from about one drop in two minutes to more than four drops per minute, whilst the blood-pressure fell at the same time from about 65 mm. Hg. to about 20 mm.

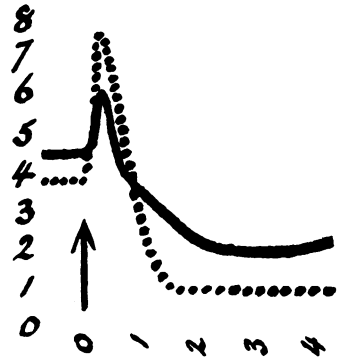

Fig. 8. Urine flow, ——— affected by stimulation of the sciatic nerve, and •••• affected by injection of adrenalin. The stimulation and injection were applied at the point indicated. Ordinate = urine in drops per minute. Abscissa = time in minutes.

Since the differences in the flow of urine dependent on the presence or absence of the suprarenals are at times out of all proportion to the differences produced in the amount of fluid flowing through the kidney vessels, it appears likely that the action of adrenalin on the kidney is not so much on the musculature of the renal vessels as on some part perhaps of the calyx or pelvis of the kidney. In this case the probable explanation of its action is that it causes some part of the pelvis of the kidney to contract, with a sudden consequent gush of urine into the bladder, and that after this initial expulsion of urine the flow of urine remains depressed as long as the contraction due to the adrenalin is maintained. This hypothesis is to a certain extent borne out by a phenomenon of common experience, viz. the effect of fright or acute nervous apprehension, in which states the bladder is frequently unable, or with difficulty able, to retain the urine suddenly poured into it. Similarly the polyuria occasionally met with in Addison's disease may perhaps be explained by the assumption that inadequacy of adrenalin brings about inadequate tonic control of the kidneys.

Two further experiments were performed in the following way: a cat anæsthetized first with A.C.E. mixture and then with urethane was eviscerated; the sciatic nerve was isolated and placed on electrodes; both ureters were catheterized with capillary tubes, and the urine was thus collected separately from the two kidneys, a drop record being taken of the flow from each: the blood-pressure was recorded from the carotid artery by a mercurial manometer in the usual way. Before the commencement of the experiment the flow of urine was increased by an intravenous injection of hypertonic saline solution. On stimulating the sciatic nerve the blood-pressure rose sharply and the flow of urine was scarcely affected (cp. Fig. 9). The left suprarenal vein was then clamped

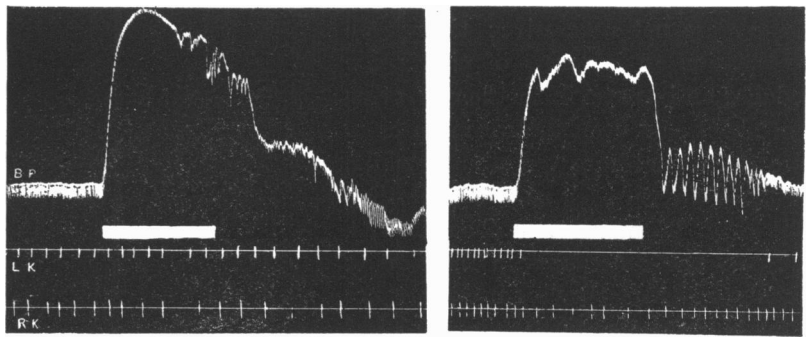

Fig. 9.

with small bulldog forceps at its point of entry into the inferior vena cava in order to prevent any of the efferent blood from the suprarenal body on that side from passing directly into the general circulation: and the urinary flow was quickened by intravenous injection of hypertonic salt solution. On stimulating the sciatic nerve once more the blood-pressure again rose sharply, the flow of urine from the right kidney as before was scarcely affected, whilst the flow of urine from the left kidney was abruptly shut off, and remained in abeyance so long as the sciatic nerve stimulation continued (shown by the band in the signal line Fig. 9) and for some time afterwards.

Summary.

1. A direct vascular connection between the suprarenal bodies (medullary portion) and the kidneys is described.

2. Under certain conditions adrenalin in appreciable amount is poured directly into the kidneys from the suprarenal bodies, producing a diminution in the flow of urine.

3. The suprarenal bodies may be regarded as direct regulators of urinary activity.