A STUDY OF THE CIRCULATION OF THE KIDNEYS FOLLOWING LIGATION OF ONE URETER.*

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In this work the perfusion box was the same as that used and described in a previous paper (1). Changes had to be made in the technique of perfusion, however, as in previous experiments only one kidney, the left, had been used.

In order to perfuse both kidneys simultaneously, two methods of procedure were tried. The first consisted in the use of one large aortic and two venous cannulæ; the second in using two arterial and two venous cannulæ. The first method, as far as it was tried, proved unsatisfactory because the serum could not be made to pass through normal kidneys at the expected rate. As the vessels given off by the aorta in this region other than the renal are very numerous, and as it was thought that the delay necessary to ligate these vessels brought about changes in the renal tissues, which probably interfered with the flow of serum, the first method was ultimately discarded. The second method therefore was the one adopted. The cannulæ used in the second method were all large enough not to impede the flow. The diameters of the outlets of both arterial cannulæ were equal, the diameters of the inlets of both venous cannulæ were equal, and the diameters of the outlets of the cannulæ protruding from the side of the box were equal. The animal to be perfused was etherized and bled to death through the left femoral vessels. The abdomen was opened, and the intestines, stomach, and liver were removed. The portion of the animal between the diaphragm and the iliac crests was then taken out, the aorta and vena cava were opened, and the cannulæ placed and ligated. The serum left the serum bottle through two glass tubes entering the arterial cannulæ under the same pressure.

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For several months the work was delayed because the serum could not be made to pass as rapidly through the right kidney as it did through the left. This discrepancy was thought to be due to technique rather than to a normal difference in the kidneys. Many possible sources of error were excluded until, finally, the discrepancy was overcome by the removal of the right adrenal.

In the rabbit the left adrenal lies almost directly over the aortic attachments of the renal arteries, and it had always been removed as it made more difficult the insertion of the cannulæ into these vessels. The right adrenal lies higher up and being less in the way had been left *in situ.*

As the removal of the right adrenal allowed the serum to pass more rapidly through the right kidney, it was thought that the removal of the left adrenal had been responsible for the ease with which the serum flowed through the left kidney. It was also thought, notwithstanding all proof to the contrary, that there might be some direct relation between the adrenals and the vasoconstrictor mechanism of the kidneys. In order to explain the above phenomena, the following experiments were performed.

RABBIT 7.

The Left Adrenal Was Left in Situ and the Right One Removed.

	Pressure.	Drops of serum. Right.[1]	Left.[1]
After 5 min.	60 mm.	120 +[2]	120 +
After 10 min.	50 mm.	100	100
After 15 min.	50 mm.	81	84

In rabbit 7 the ligature around the left arterial cannula had been placed between the adrenal and the kidney. As the presence of the left adrenal did not seem to interfere with the rate of flow, it was thought that perhaps this ligature might have destroyed the relation between the adrenal and kidney on this side. The following experiments were therefore performed.

[1] The figures under the words "right" and "left" represent the number of drops of serum issuing in one half minute from the cannulæ protruding from the side of the perfusion box.

[2] It was found impossible to count accurately over 120 drops in 30 seconds. In such cases, therefore, where the serum issued from the cannulæ in distinct and separate drops, yet at a rate faster than 120 per 30 seconds, the sign 120 + was used.

RABBIT 19.

	Pressure.	Drops of serum. Right.	Left.
After 5 min.	40 mm.	95	120+
After 8 min.	40 mm.	100	120+
After 10 min.	40 mm.	90	120+
Right adrenal removed.			

RABBIT 21.

	Pressure.	Drops of serum. Right.	Left.
After 3 min.	40 mm.	85	120
After 5 min.	40 mm.	80	120
After 8 min.	40 mm.	80	120+
Right adrenal removed.			
After 10 min.	40 mm.	120	120+
After 15 min.	40 mm.	120+	120+

In these rabbits the ligatures around the arterial cannulæ were placed between the adrenals and aorta. During the first part of the experiment both adrenals were left *in situ*. During the latter part, the right adrenal was removed. In rabbit 19 air entered the right arterial cannula after the removal of the adrenal and the latter part of this experiment was consequently discarded.[3]

Having found a method whereby the serum could be made to flow simultaneously through both kidneys with the same pressure, at the same rate, two normal rabbits, each of which weighed between 1,500 and 2,000 grams, were perfused. The following results were obtained.

RABBIT 3.

	Pressure.	Drops of serum. Right.	Left.
After 5 min.	60 mm.	100	100
After 10 min.	50 mm.	103	100
After 15 min.	50 mm.	100	100

RABBIT 20.

	Pressure.	Drops of serum. Right.	Left.
After 5 min.	40 mm.	120	120
After 10 min.	40 mm.	120	120
After 15 min.	40 mm.	120	120

The flow through the normal kidneys in this series is apparently more rapid than that obtained previously (1), but this is explained by the small outlets to the cannulæ protruding from the side of the perfusion box, and the consequently smaller and more frequent drops.

In order to exclude nephropathic kidneys, only those rabbits were used the urine of which was free from albumen. Despite this, many of the rabbits on being opened were found to have diseased kidneys. In most of these rabbits the operation was continued and a ureter was tied as it was thought that the changes in nephropathic kidneys might be different from those in the normal kidney.

[3] Further attempts will be made to determine the exact relation between the adrenal gland and kidney perfusion.

In order to ligate the ureter the rabbits were etherized, the abdomen was opened, either the right or left ureter was ligated with silk, and the abdomen was then closed. Complete aseptic precautions were observed throughout. Several of the animals operated on died a few days after operation. The cause of death in these animals was not ascertained (2). It may be said, however, that the majority of the rabbits that died were from those that had changes in the kidney prior to ligation of the ureter.

With the object in view of finding out whether the intrapelvic pressure brought about by ligation of the ureter impeded circulation through the kidney (3) and whether this impediment gave rise to a compensatory increase in the flow through the other kidney, the first two rabbits operated on that were found to be normal were allowed to live three weeks before being perfused. Of these two animals, the hydronephrotic kidney of rabbit 1 was found to have become infected and consequently the changes produced therein by pressure could not be determined. The opposite kidney, however, other than being decidedly hypertrophied, showed no infection. Therefore, the animal was perfused with an idea of determining whether the flow through the hypertrophied kidney had materially increased. Rabbit 3 showed no infection.

RABBIT 1.

Right Ureter Ligated.

	Pressure.	Drops of serum. Right.	Left.
After 5 min.	40 mm.	5	Stream.[4]
After 10 min.	40 mm.	5	Stream.

RABBIT 3.

Left Ureter Ligated.

	Pressure.	Drops of serum. Right.	Left.
After 3 min.	40 mm.	Stream	0
After 5 min.	120 mm.	Pressure shut off	60
After 7 min.	60 mm.	Stream	14
After 10 min.	60 mm.	Shut off	16
After 14 min.	60 mm.	Shut off	14
	Sac punctured.		
After 14 min.	60 mm.	Stream	40
After 20 min.	60 mm.	Stream	48
After 25 min.	60 mm.	Stream	48

The conclusions drawn from the above experiments are as follows: (1) The intrapelvic pressure produced by ligation of a ureter impedes circulation through the kidney. (2) At the end of three

[4] Serum drops of approximately over 175 per minute lost their identity and merging formed a stream. In such cases the word "stream" is used.

weeks there is a compensatory increase in the rate of flow through the vessels of the opposite kidney. (3) At the end of three weeks after ligation of the ureter, changes occur in the kidney tissue which in themselves are sufficient to impede circulation.

On arriving at the above conclusions, the following experiments were performed with the object in view of determining how soon after ligation of the ureter the changes in the kidney tissue became sufficiently developed to produce an impediment to the flow. In this series the perfusion of the rabbits was begun as heretofore. When the flow through both kidneys had reached its maximum rate, the hydronephrotic sac was punctured and the perfusion then continued until the flow through the damaged kidney had again reached its maximum.

RABBIT 15.

Perfused Twenty-Four Hours after Ligation of Left Ureter.

	Pressure.	Drops of serum. Right.	Left.
After 5 min.	60 mm.	120 +	9
After 8 min.	60 mm.	120 +	9
	Sac punctured.		
After 10 min.	60 mm.	120 +	10
After 15 min.	60 mm.	120 +	10

For lack of serum the experiment was here discontinued.

RABBIT 12.

Perfused Forty-Eight Hours after Ligation of Left Ureter.

	Pressure.	Drops of serum. Right.	Left.
After 5 min.	60 mm.	120 +	2
After 10 min.	60 mm.	120 +	2
	Sac punctured.		
After 13 min.	60 mm.	120 +	9
After 18 min.	60 mm.	120 +	78
After 20 min.	60 mm.	120 +	112
After 25 min.	60 mm.	120 +	120 +

RABBIT 13.

Perfused Forty-Eight Hours after Ligation of Right Ureter.

	Pressure.	Drops of serum. Right.	Left.
After 5 min.	40 mm.	9	120 +
	Sac punctured.		
After 10 min.	50 mm.	90	120 +
After 15 min.	40 mm.	120 +	120 +

RABBIT 14.

Perfused Seventy-Two Hours after Ligation of Left Ureter.

	Pressure.	Drops of serum. Right.	Left.
After 3 min.	60 mm.	Stream	13
After 5 min.	40 mm.	Stream	10
After 8 min.	60 mm.	Stream	28
After 10 min.	60 mm.	Stream	42
After 12 min.	40 mm.	Stream	70
After 15 min.	40 mm.	Stream	70
	Sac punctured.		
After 20 min.	40 mm.	Stream	120

For lack of serum the experiment was here discontinued.

RABBIT 17.

Perfused Ninety-Six Hours after Ligation of Right Ureter.

	Pressure.	Drops of serum. Right.	Left.
After 2 min.	60 mm.	70	120 +
After 5 min.	60 mm.	120	50
After 10 min.	50 mm.	120 +	50
Sac punctured.			
After 12 min.	50 mm.	120 +	80
After 15 min.	60 mm.	120 +	120

RABBIT 18.

Perfused Ninety-Six Hours after Ligation of Left Ureter.

	Pressure.	Drops of serum. Right.	Left.
After 5 min.	60 mm.	120	40
After 8 min.	40 mm.	Stream	50
After 10 min.	60 mm.	Stream	50
Sac punctured.			
After 14 min.	60 mm.	Stream	60
After 16 min.	60 mm.	Stream	55
After 20 min.	60 mm.	Stream	50

RABBIT 16.

Perfused One Week after Ligation of Right Ureter.

	Pressure.	Drops of serum. Right.	Left.
After 2 min.	60 mm.	21	Stream.
After 5 min.	60 mm.	15	Stream.
After 6 min.	40 + mm.	6	120 +
	Sac punctured.		
After 10 min.	60 mm.	26	Stream.
After 12 min.	60 mm.	30	Stream.
After 14 min.	80 mm.	80	Shut off.
After 20 min.	80 mm.	82	Shut off.
After 22 min.	60 mm.	60	Shut off.
After 25 min.	60 mm.	60	Shut off.

Summary.—Increased intrapelvic pressure impedes the flow of serum through the kidney. Following ligation of the ureter a change occurs in the kidney tissues which offers an impediment to circulation other than that produced by pressure alone; this change

occurs one week after ligation. A compensatory increase in the rate of flow through the control kidney is first noticed seventy-two hours after ligation and is quite apparent at the end of one week.

HISTOLOGY.

The histological changes following ligation of the ureter have been described by many investigators (4, 5, 6). The changes will be described here in as far as they seem to be related to the problem in hand.

RABBIT 15.

Perfused twenty-four hours after operation.

Control Kidney.—No change is seen other than a slight edema associated with perfusion. A few of the glomeruli are distended with blood showing that the perfusion had not extended equally over all parts of the kidney.

Kidney with Ligated Ureter.—This kidney shows dilatation of all the convoluted and particularly the large collecting tubules near the end of the pyramids. Many of the tubules of Henle particularly the descending loops contain definite casts both hyaline and granular. Some are also found in the collecting tubules. In the cortex the primary convoluted tubules show slight swelling. Very considerable changes consisting in exudation and cell desquamation are found in the secondary tubules. None of these lesions are equally distributed; although there is general degeneration of the epithelium, the changes are more marked in single groups of tubules. The glomeruli are intact. The perfusion in this kidney is not complete, as many of the straight vessels in the pyramids contain blood. There is also much blood in the capillaries of the cortex.

RABBIT 13.

Perfused forty-eight hours after operation.

Control Kidney.—In this kidney the epithelium of the tubules in the pyramids is normal; the tubules are not dilated. There is an occasional cast in the Henle loops, and considerable edema. There is considerable edema in the tubules of the cortex with granular material in the lumen. Around all the glomeruli there is a crescent of coagulated exudation which consists in a granular mass enclosing large hyaline droplets. The perfusion here extended to all the glomeruli, the kidney being completely bloodless. This kidney is not absolutely normal, there being a few foci of cell infiltration and connective tissue increase in the cortex. The granular material in the convoluted tubules here is the same as that in the capsular spaces. The globules are usually of the same size and show a completely hyaline mass within a definite circle.

RABBIT 12.

Perfused forty-eight hours after operation.

Control Kidney.—This shows material of the same character in the capsular space, but very much smaller in amount and the hyaline globules are not so

marked. It is difficult in these cases to decide whether the material in the capsular space is due to perfusion and represents material which during the perfusion has passed through the glomeruli, or whether it had occurred during life. In many cases it is so abundant that the glomerulus is apparently compressed by it. The fact that it is not a condition common to a perfusion would seem to be evidence that it occurred during life, although it is perfectly possible that in these kidneys the glomeruli may have become more permeable.

Kidney with Ligated Ureter.—There is some dilatation of the collecting tubules, as in the previous case. Casts are present, but they are not so numerous in the tubules of the pyramids. The epithelium of the pelvic tubules shows a greater degree of degeneration, and the dilatation involves the smaller tubules of the pyramids relatively more than the larger. The dilatation involves also the tubules of the cortex, and in places even the primary collecting tubules. The secondary tubules are often dilated to double or more of the normal lumen. The epithelial degeneration in the primary convoluted tubules is well marked, and the tubules contain granular material derived from the epithelium. The most striking thing in this kidney is the greater extension of the dilatation into the tubules of the cortex.

RABBIT 14.

Perfused seventy-two hours after operation.

Control Kidney.—In this case the glomeruli are large and there is a varying amount of the same material in the capsule. Some contain a great deal, others but a small amount. In this kidney many of the glomeruli contain blood and have escaped the perfusion; elsewhere, there is much the same condition as in the kidney previously examined.

Kidney with Ligated Ureter.—The usual condition of dilatation of ducts and degeneration is seen. There is very little difference from that seen in the former kidneys.

RABBIT 16.

Perfused one week after operation.

Control Kidney.—In this kidney the exudate in the capsules is present. The epithelium generally is large and granular. There is some edema.

Kidney with Ligated Ureter.—There is the usual tubular dilatation. In the pyramids there is a distinct increase in connective tissue around the small blood vessels. There is throughout the kidney in both pyramids and cortex an increase in connective tissue. The glomeruli contain no exudate, but show an increase in the vascular cells which varies in degree.

RABBIT 3.

Perfused twenty days after operation.

Control Kidney.—The glomeruli on being measured are generally found to be larger than normally. Around most of them there is some granular material. The convoluted tubules show large, well granulated cells, and here and there in the pyramids there are foci of cellular infiltration.

Kidney with Ligated Ureter.—The dilatation of tubules here is but slightly apparent. There is a very marked increase of tissue with masses of cell infiltration in the pyramids, apparently extending from this into the cortex. The

increase of tissue in the cortex is diffuse, but accentuated in foci, and the dilatation of tubules is relatively more marked in the small collecting tubules of the cortex than elsewhere. There is marked thickening and proliferation of the epithelium of the cortex.

SUMMARY.

During the first four or five days after ligation of the ureter, the changes in the kidney are mainly degenerative in type. One week after ligation of the ureter connective tissue cells begin to appear infiltrating the kidney tissues. There is also an increase in the vascular cells of the glomeruli. These changes are well marked at the end of twenty days from the time of ligation. At the end of twenty days from the time of ligation there is also a marked hypertrophy of the control kidney, the glomeruli showing an average increase in size of twenty-five microns.

CONCLUSIONS.

During the first week following ligation of one ureter there is found an impediment to circulation which is removed upon opening the distended pelvis and reducing the intrapelvic pressure. This impediment, therefore, is probably due to the compression of the blood vessels within the kidney brought about by dilated tubules and unyielding capsule, and also possibly to disturbance of circulation produced by the distension of the pelvis. The venous and arterial branches passing over this may be either compressed or in various ways distorted. During this period the anemia produced by the impediment together with pressure and other factors gives rise to changes in kidney tissues which reveal themselves microscopically as a swelling and degeneration of the epithelial cells. Cloudy swelling was found by Karsner and Austin (7) two hours after experimental bland embolism of the renal artery.

At the end of one week following ligation of one ureter there is an impediment to the circulation other than that due to intrapelvic pressure. This impediment is probably due to cicatricial changes in the organ, which tend to maintain the tubules dilated and in a position of encroachment on the space normally allotted to blood vessels, and which manifest themselves microscopically as a connective tissue cell infiltration into the interstitial tissues of the

kidney, and an increase in the vascular cells of the tufts diminishing the caliber of the tuft capillaries.

The increased amount of work thrown upon the control kidney produces no lesions other than a hypertrophy, which permits a greater and more rapid circulation through its vascular system.

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