

Experimental Pyelonephritis and Hypertension in Rats.* (18919)

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The occurrence of chronic and healed pyelonephritis and the development of arterial hypertension have been shown to be correlated by analysis of clinical material(1,2). Experiments with animals have contributed information concerning the pathogenesis of chronic pyelonephritis(3). To our knowledge the occurrence of arterial hypertension in animals with experimentally induced pyelonephritis has not been demonstrated. Heretofore rabbits have usually been employed in the experimental study of pyelonephritis. The technical advantages offered by the size of these animals are offset by considerations of economy and space. Therefore, a smaller animal was chosen for this study. The use of rats seemed feasible because pyelonephritis develops spontaneously in them(4). Furthermore, rats have been shown to develop hypertension under several experimental conditions(5).

The purposes of this investigation were (1) to develop a technic for the production of pyelonephritis in the rat; (2) to ascertain what changes occur in the arterial blood pressure of rats with experimentally induced pyelonephritis.

Methods. Sixteen white rats weighing about 250 g were used in these experiments. In principle the technic of producing pyelonephritis was similar to that used by Mallory(3). An incision was made in the left flank of a rat under anesthesia. The left

ureter was partially mobilized, maintained intact, and a "U" shaped segment passed through the incision in the flank. This segment was maintained in position by a 1.5 cm length of wire passed through the "U" and allowed to rest against the outer muscle layer of the abdominal wall. The muscles were then sutured loosely about the ureter and the skin closed with wound clips. Twenty-four hours or more after the procedure a suspension of viable *Escherichia coli*[†] was injected into the vein of the tail in a volume of 1 cc. The number of viable organisms injected was determined by a standard counting technic. The "systolic" arterial pressure of each animal was determined by the method of Kersten *et al.*(6) on several occasions preceding and following operation and infection. In a few a Hamilton optical manometer was employed. In some cases examination of the urinary sediment and culture were made. At intervals the animals were sacrificed and examined. Microscopic sections of the kidneys were made. The infected kidneys were cultured for bacteria. In two instances the ligature was removed before the injection of the bacteria.

Results. The results are shown in Table I. Five animals received a dose of viable *E. coli* in excess of 3.0×10^9 organisms. Of these 4 died within 4 days after injection without hypertension developing. Three were found to have definite evidence of acute pyelonephritis as well as early hydronephrosis and hydroureter of the experimentally obstructed kidney. Another (rat 2) had early hydronephrosis of the kidney operated on but little evidence of pyelonephritis. One (rat 1) survived and at autopsy 127 days later was

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1. Longcope, Warfield T., *Ann. Int. Med.*, 1937, v11, 149.

2. Weiss, Soma, and Parker, F., *Medicine*, 1939, v18, 221.

3. Mallory, G. K., Crane, A. R., and Edwards, J. E., *Arch. Path.*, 1940, v30, 330.

4. Wilens, S. L., and Sproul, E. E., *Am. J. Path.*, 1938, v14, 201.

5. Schroeder, H. A., *J. Exp. Med.*, 1942, v75, 315.

[†] This organism was isolated from urine of a pregnant woman with severe pyelonephritis.

6. Kersten, H., Brosene, W. G. H., Ablondi, F., and Subbarow, Y., *J. Lab. and Clin. Med.*, 1947, v32, 1090.

TABLE I. Experimental Pyelonephritis in Rats.

	Rat No.	Autopsy performed		Dose <i>E. coli</i> i.v. $\times 10^9$	Blood pressure (mm Hg)		Autopsy findings, left kidney (Microscopic)					Remarks
		Days after infection	Days after operation		Pre-op.	Ante-mortem	Gross	Culture	Pyelonephritis	Vascular disease in both	Bacilluria, days after infection	
Hypertensive	7	41	46	1.6	101	167	Hn. Hu.	+	—	—		Died
	13	48	51	1.9	—	180	" "	+	—	—		
	14	44	47	.55	—	(207/172)* 172	" "	+	+	+	3	
	8	104	110	1.6	98	(159/121)* 185	Pyn. Pyu.	+	+	+	3	
	12	104	112	1.6	107	159	" "	+	+	+	18	
	9	106	112	1.6	109	154	Contracted	0	+	+		
	10	106	112	1.6	100	153	"	0	+	+	18	
	15	48	51	2.9	—	168	"	+	+	+		
	1	127	133	18	120	(181/137)* 168	1 scar	0	1 area	+	35	
	2	4	12	18	110	110	Hn. Hu.	+	+	0	3	Died
Normotensive	3	1	5	5	115	92	" "	+	+	—		"
	4	1	5	5	115	99	" "	+	+	0		"
	6	1	9	5.2	110	103	" "	+	—	—		"
	16	48	51	2.9	—	100						L.R. day 2†
	17	44	47	1.9	—	(77/49)* 108	N	0	0	0	3	" " "
						(75/41)* 110	N	0	0	—	3	" " "
	11	—	112	None	113	110	N	0	N	—		" " "

* Hamilton manometric reading under anaesthesia.

† L.R. = ligature removed.

Hn. = hydronephrosis. Hu. = hydroureter. Pyn. = pyonephrosis. Pyu. = pyoureter. N = normal. — = not examined.

found to have no hydronephrosis but an area of pyelonephritis in that kidney which had been subjected to surgery.

Three animals (rats 9, 10, and 15) given smaller doses of *E. coli* were found to have very scarred and contracted left kidneys. The blood supply of these kidneys appeared not altered from the normal and evidence of hydronephrosis and hydroureter was not present. In two animals (rats 9 and 10) the infection was apparently "healed" as cultures of the affected kidneys grew out no organisms. Microscopic examination of these specimens revealed marked destruction of renal tissue, scarring, and inflammatory cellular infiltration. "U" shaped wedges of surprisingly normal appearing glomeruli persisted in each left kidney. The contralateral kidneys were essentially normal except for vascular changes. The blood pressure of these animals was consistently elevated above control levels.

Five animals which survived infection with less than 2.0×10^9 viable *E. coli* were sacri-

ficed 44 to 104 days following infection. Two (rats 8 and 12) displayed a striking pyonephrosis and pyoureter on the left side. Microscopic examination of the pyonephrotic kidneys revealed advanced destruction of the renal parenchyma, scarring, and cellular infiltrations of inflammatory character. The only remaining structures recognizable as renal tissues were a few intact glomeruli. Except for microscopic vascular changes the contralateral kidneys were within normal limits. Three (rats 7, 13 and 14) developed moderate to marked hydronephrosis and hydroureter with infection in the renal parenchyma; cultures grew out *E. coli*. The blood pressures of these animals were consistently elevated above the control levels.

In two cases (rats 16 and 17) the wire retaining ligature was removed before the injection of *E. coli* was made; in neither case did pyelonephritis or hypertension develop. In another (rat 11) the operation alone was performed without subsequently injecting *E. coli*.

The wire retaining ligature was removed two days after operation. Hypertension did not develop and at autopsy the left kidney was within normal limits.

Vascular changes in the right unoperated kidney were observed in the animals with hypertension of several weeks' duration. This was usually less in degree from that observed in the infected kidney, but was easily demonstrable. In only one animal was it marked (rat 1).

Discussion. There were 3 findings of interest in these experiments. First, hypertension of some degree invariably accompanied chronic unilateral pyelonephritis in the rats surviving the infection. Hypertension has been induced by unilateral hydronephrosis alone(5) when the kidney was not totally destroyed, but unfortunately superimposed infection was not ruled out. Secondly, in some instances contracted, fibrotic, pyelonephritic kidneys showing no hydronephrosis resulted

from partial ureteral obstruction and infection. Thirdly, only the kidney in which there was ureteral or pelvic stasis became infected, a circumstance which might have been predicted(3). In addition, vascular changes in the opposite kidney were seen in those animals which developed hypertension, also a predictable finding(7).

The method used was simple and readily applied. Further studies on prevention or treatment of the pyelonephritis so induced should be rewarding.

Summary. Unilateral renal diseases resembling hydronephrosis, pyonephrosis, or pyelonephritis were induced in rats by partial ureteral constriction and intravenous injection of *E. coli*. Arterial hypertension developed when chronic unilateral renal infection was produced.

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A Technic for Measurement of Radioactive Iodine (I-131) Uptake by the Human Thyroid Gland. (18920)

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In the study of the uptake of iodine (I-127) by the thyroid, the most practical tracer is the radioactive isotope of iodine (I-131). This isotope has a half life of 8 days and emits 2 types of radiation, beta particles and gamma rays. The maximum energy of the emitted betas is of the order of 600 Kev, while the gammas are emitted with a maximum energy of 723 Kev(1). The conventional Geiger-Muller tube is 90% efficient in measuring beta radiation and only 2% efficient for the gamma radiation. This means that of the incident radiation, 90% of the beta radiation and 2% of the gamma radiation will be re-

corded. The tube used in our work is a bismuth cathode, Geiger-Muller tube, Radiation Counter Laboratories, Mark 1, Model 12, used axially like an end window counter. The tube has a high gamma efficiency and a low beta efficiency. In an actual comparative experiment using I-131 the bismuth cathode tube showed a count rate of about 7.5 times greater than the conventional end window tube over the same sample. To attain the same counting geometry, the end window tube must be recessed about 1 inch into the lead shield. With this change in tube distance, the bismuth tube count rate is 11 times greater. With the beta radiation filtered out by appropriate aluminum absorbers, the ratio of count rates increases to approximately 16 times. Since most of the beta radiation is

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