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THE VESICORENAL REFLEX IN THE PATHOGENESIS OF UREMIA

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THE VESICORENAL REFLEX IN THE PATHOGENESIS OF UREMIA

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INTRODUCTION

The role of urinary tract obstruction in reversible uremic states has become increasingly recognized in recent years. Decrease in renal function in lower tract obstruction is generally appreciated, but the pathogenesis of the reversible changes is not fully understood.

Obstruction to urinary flow anywhere along the urinary tract can lead to renal failure. It has been established that in older individuals (65 yr. - 83 yr.) renal function is diminished to about 75% of that of normal young men (20 yr. - 39 yr.).[13] Prostatic or bladder neck obstruction in the elderly patient may aggravate the existing renal impairment and compromise renal function sufficiently to precipitate an episode of azotemia. The impairment of renal function might be explained on the basis of an increased hydrostatic pressure on the kidney leading to an increase in intratubular pressure and to a reduction in the glomerular filtration rate.[6] A rise in intratubular pressure may also lead to an increase in the peritubular capillary pressure causing a decrease in effective renal blood flow which may be a major factor in early azotemia. It has been observed that as the degree of prostatic obstruction advances there is bladder hypertrophy with an increased intravesical pressure.[4] This elevated intravesical pressure may cause obstruction of urine flow from the ureter into the bladder even in the presence of a competent ureterovesical valve mechanism.[15] It has been observed in patients with chronic urinary retention associated with early azotemia that a rapid and remarkable improvement may occur when the bladder is drained.[2]

This suggests that the oliguria may be due to a reflex inhibition of renal function as a result of distention of the lower urinary tract.

Reflex inhibition of urine flow has been produced in several ways. Instrumentation of the lower urinary tract in man may cause acute urinary suppression.[21,25] It has been postulated that painful physical and psychic stimuli can inhibit urine flow by either depression of renal blood flow, presumably due to autonomic responses, or the liberation of anti-diuretic hormone (ADH).[16, 24] It has recently been suggested that obstruction of the ureteral orifices by focal bullous edema of the bladder mucosa following ureteral manipulation is probably the cause of urinary suppression after catheterization.[21] In rabbits and cats it has been observed that a reduction in renal clearance follows electrical stimulation of the sciatic nerve.[1] An alteration of vascular tone in the renal cortical circulation or the presence of an active shunting of blood through the juxtramedullary glomeruli, described by Trueta, was thought to be responsible. Electrical stimulation in rabbits of the lower ureter, vesical neck, lumbar spinal cord, and the nerves of the renal pedicle also produced reflex suppression of urine for at least twenty minutes.[23] Denervation of the kidney abolished the response to electrical stimulation. It was concluded that any stimulus of sufficient intensity can produce a reflex oliguria mediated by the autonomic nervous system. Unilateral high frequency stimulation of the nerves around the renal pedicle in dogs has been shown to decrease urine flow significantly while flow from the un-

stimulated kidney remained relatively constant.[7] This is thought to produce renal ischemia due to sympathetic vasoconstriction and be responsible for the reflex anuria.[5]

Seres stated in 1923 that the reduced urine flow associated with bladder distention, which he had observed, was probably due to pain.[18] As mentioned previously, pain can stimulate ADH release causing oliguria. It has been observed in dogs with an intact urinary system that distention of the bladder, as well as pelvic nerve stimulation, inhibited urinary flow.[3] This was abolished by section of the splanchnic nerves which suggested the possibility of a vesicorenal reflex. It was postulated that the efferent phase of the reflex arc is via the spanchnic nerves. Negative pressure applied to the bladder has been shown to increase urine flow for at least ninety minutes, whereas positive pressure was associated with a reduction in flow.[11] These observations are open to criticism as no methods are given and negative pressure as applied to an empty bladder, a potential space, is unphysiological.

The effect of increased ureteral pressure on renal function in an intact urinary tract has also been studied by means of direct ureteral catheterization. A persistent unilateral inhibition of urine flow was observed with a moderate increase of intraureteral pressure produced by raising the end of the ureteral catheter on one side to the desired height.[17] The reduction in urine volume paralleled the reduction in sodium excretion during the period of increased ureteral pressure. It was suggested that the glomerular filtration rate is lowered and the reduced solute load is more

completely reabsorbed in the renal tubules. A slowing of the urine flow which allowed more time for reabsorption of electrolytes and water is an alternative explanation. The decrease in renal function secondary to an increase in ureteral pressure has been confirmed and it was found that it could not be abolished by sympathetic blockade with drugs.[19] Variations of pressure in an isolated segment of ureter do not affect renal function.[11, 19]

These experiments indicate that bladder distention or increased ureteral pressure, in an intact urinary system, leads to a reduction in urine output. The results could be explained in most cases on the direct or indirect effects of hydrostatic back pressure of the kidney. Other factors, especially the release of ADH, could account for reduced renal function. Although the autonomic nervous system does not appear to be responsible for a decreased urine output secondary to increased ureteral pressure, there is evidence that the activation of autonomic reflexes can cause renal suppression. The data in these experiments did not exclude the possibility that bladder distention led to a reduction in urine output by means of a neurogenic mechanism. A situation in which the phenomenon of bladder distention could be studied without the effects of hydrostatic back pressure on the kidneys would help to clarify this point.

During an investigation of the dynamics of acute urinary retention in the dog, in which there were no mechanical connections between the bladder and the

kidneys, it was noted that the urine output was significantly diminished during periods of bladder distention.[9] In this experiment the ureters were sectioned near the bladder and the proximal ends were brought outside of the dog's abdomen. Since there were no connections between the bladder and the kidneys, it was suggested that the oliguria was due to vesicorenal reflexes.

Various experiments have been carried out since to confirm these incidental observations.[8, 9, 12, 22] The basic experimental model involves the sectioning and cannulation of the ureters (See Fig. 1). There are no hydraulic connections between the bladder and the kidneys through which back pressure might be exerted. It has been concluded that an increase of intravesical pressure within physiological limits results in a decrease of urine production by the kidneys. These conclusions do not appear justified based on the experimental evidence presented because standard conditions of renal function were not attained during these experiments.

The present study was undertaken to investigate whether there is a mechanism which regularly inhibits urinary output when the bladder is distended. In order to achieve standard and comparable conditions, it is important to maintain a constant diuresis with urea. Because constant water reabsorption is desirable, comparative studies on urine flow should be in the presence of maximal ADH stimulation. This would prevent changes in renal function due to endogenous ADH release from pain stimuli.

It has been observed that in the patient with prostatic obstruction there is frequently a decrease in renal function.[14] It is known that this may improve considerably after the relief of obstruction, but there is conflicting evidence as to which aspects of renal function are restored.[10, 14] A study was undertaken in which renal function was estimated in a group of patients before and after relief of benign prostatic obstruction by surgery. This was done in an attempt to obtain a better understanding of the pathogenesis of uremia and to determine whether there was any correlation between the experimental results and the clinical findings.

MATERIALS AND METHODS OF ANIMAL EXPERIMENTS

Male dogs averaging twenty kg. in weight, anesthetized with sodium pentothal (25mg/kg IV) were used in these experiments. When the abdominal incision was closed, analgesia was maintained with morphine (0.5mg/kg IV) during the remainder of the experiment, so that the dogs were unanesthetized during the time that observations were being made on urine flow.

A continuous intravenous infusion of 5% Dextrose and water was administered during the surgical procedure to ensure adequate hydration of the animals. The ureters were exposed transperitoneally through a midline suprapubic incision and dissected free about seven cm. from the bladder. A small longitudinal incision was made into each ureter and polyethylene catheters (#190 O.D. .067") were introduced proximally and distally (See Fig. 1). The proximal catheters were advanced until they were within the renal pelves, and then a ligature was applied around the ureters to hold the catheters in place. Urine output per minute was measured from the free ends of each of the proximal catheters draining the kidney. The distal catheters were advanced through the ureters into the bladder and similarly secured. The free end of one of these was connected to an infusion system which could deliver physiological saline into the bladder at a constant rate. The abdominal incision was closed with tension sutures. A polyethylene catheter (#280 O.D. .128") was passed into the bladder through the urethra and was connected to a mercury mano-

meter to monitor the intravesical pressure. The arterial pressure was monitored continuously through a catheter placed in the carotid artery in the neck.

Standard and comparable conditions of renal function were obtained by producing a diuresis with urea and maximal tubular reabsorption of water with anti-diuretic hormone (ADH). A constant high concentration of ADH was administered to obviate changes in urine output due to the production of endogenous ADH. An initial loading dose of ADH (50mu/kg) was administered intravenously at the beginning of the experiment. Once the catheters were in place, a continuous infusion of a solution of 8% urea in normal saline and ADH (50mu/kg/hr) was given at a rate of 2.25ml/min using a finger infusion pump.

Thirty to sixty minutes after the abdominal incision was closed, conditions became stabilized and the urine output remained constant. The experiment consisted of a ten minute control period. This was followed by filling the bladder with saline at a constant rate for a period varying from 5 to 135 minutes. The rate of infusion into the bladder, usually one to three times the dog's urine output, provided for a steady, but slow, increase in bladder pressure. Rapid distention of the bladder, with its accompanying large changes in bladder pressure, was avoided. Some bladder accommodation to the increasing volume occurred, but the slow infusion gradually produced a rise in intravesical pressures from between 20 to 40 mm Hg. A recovery period followed when the bladder was allowed to empty. Blood pressure and bladder

pressure were monitored continuously throughout the experiment. Urine output per minute for each kidney was measured during all three periods. Samples of urine for measurement of osmolarity were taken from each kidney during the control, experimental, and recovery periods. The osmolarity was determined with a freezing point osmometer. In one dog (#4) the glomerular filtration rate (GFR) was estimated by means of a creatinine clearance test. Simultaneous blood and urine samples were taken during the control, experimental, and recovery periods.

The effects of ureteral distention were obtained in the following manner. The surgical procedure was as described for the above experiments. A ureteral catheter (#4) with a small inflatable balloon was introduced into one of the distal ureters and held in place with a ligature. An 8% urea-saline-ADH solution was infused at a constant rate. The experiment consisted of a 10 minute control period during which the urine output remained steady. This was followed by a 10 minute experimental period during which the pressure in the ureteral lumen was raised by distention of the balloon. Release of pressure in the ureteral segment was followed by a 10 minute recovery period. Blood pressure was monitored continuously and urine output per minute from each kidney was measured throughout the experiment.

RESULTS OF ANIMAL EXPERIMENTS

The effect of increased bladder pressure was observed in 7 dogs in whom 17 experiments lasting from 5 to 135 minutes were carried out. It was found that a sustained decrease in urine output occurred during the periods of increased intravesical bladder pressure. This was observed first as the bladder pressure was raised to 15 mm Hg. (See Graphs I-VIII). A further increase in bladder pressure was associated with a further decrease in urine output (Graph IX). The response was similar in the two kidneys. Urine output during the experimental periods as compared both to the control and recovery periods showed a decrease of between 5 to 58%. (Table I). Release of bladder pressure was followed by a prompt return in urine output to previous levels during the recovery period.

While there was a definite alteration in urine output associated with changes in bladder pressure, it appeared to have no relationship to bladder volume. A large bladder volume (200cc) with an intravesical pressure below 15 mm Hg. did not result in a reduction in urine output, whereas an increase in bladder pressure, even with a small volume of fluid, was consistently related to decreased urine production.

There were no significant changes in osmolarity of the urine collected during the control, experimental, or recovery periods, which would indicate that the changes in output were due to variations in the glomerular filtration rate and were not the result of increased tubular reabsorption. In two experiments on dog #4 the

creatinine clearance was calculated in order to estimate changes in GFR during the experimental periods. Creatinine clearance was decreased from a control level of 74.6 ml/min to 55.7 ml/min during periods of bladder distention. This represented a significant decrease of 25% in creatinine clearance. In the recovery phase the creatinine clearance rose to 79.0 ml/min. It seems quite likely that the diminished GFR is responsible for the reflex oliguria.

There was no significant variation in blood pressure during any of the experiments, except in dog #5 when the systemic pressure rose 10 mm Hg. as the bladder was distended.

While the urea-saline-ADH solution was infused during most experiments, several experimental periods were conducted with a urea-saline solution. The inverse relationship between urine output and bladder pressure was observed consistently and it appears that the addition of ADH to the infusate produced a more marked reduction in urine output during periods of increased bladder pressure. (Table 1).

Pressures averaging 120 mm Hg. were maintained for 10 minutes within the ureteral lumen. No changes in urine output were observed following an increase in intraureteral pressure of between 90 and 140 mm Hg. for periods up to 10 minutes.

MATERIALS AND METHODS OF CLINICAL STUDY

Eleven men with chronic urinary obstruction due to benign prostatic enlargement were investigated. The average age was 65 (range 55 - 79 yr.). The presenting symptoms were frequency, dysuria, and overflow continence due to urinary retention. An intravenous pyelogram and cystoscopy were performed prior to surgery. Three different operative procedures were used in this group of patients: transurethral resection (5); suprapubic prostatectomy (5); and retropubic prostatectomy (1). All eleven patients were discharged from the hospital within two weeks following surgery.

The tests of renal function were done on all patients in the preoperative phase and repeated from between 4 to 62 days after surgery (mean of 18 days). A twelve hour urine collection (8:00 P.M. - 8:00 A.M.) was used for determining urine volume, urine osmolarity, and urinary creatinine. Blood was obtained for determining the blood urinary nitrogen (BUN), serum electrolytes, and serum creatinine. The glomerular filtration rate (GFR) was estimated by means of a twelve hour creatinine clearance test.

A test response to exogenous ADH was undertaken in 8 patients before and after relief of obstruction. Pitressin tannate in oil (5 units of ADH) was injected intramuscularly before midnight and the osmolarity of the first morning specimen was determined. In patients on catheter drainage, urine osmolarity was estimated

from a urine specimen collected between midnight to 8:00 A.M. Due to difficulties with residual urine and catheter drainage, a phenosulfonphthalein (PSP) test could be performed accurately on only three patients before and after surgery.

RESULTS OF CLINICAL STUDY

Studies of renal function were undertaken in eleven elderly patients with lower urinary tract obstruction due to benign prostatic hyperplasia. Pre-operative evaluation included an intravenous pyelogram which indicated good bilateral kidney function in all cases. Cystoscopy revealed a large, trabeculated bladder in the majority of cases. Three of the eleven patients (#6, 7, 8) required pre-operative catheter drainage because of urinary retention (average amount of residual urine - 770 cc). Only two patients (#7, 8) had an elevated BUN prior to surgery. Serum electrolytes were within normal limits for all the patients.

The GFR, as measured by creatinine clearance, was estimated successfully in all cases. (See Table II). The average creatinine clearance was 64 ml/min post-operatively. There was an increase in 7, a decrease in 2, and no change in 2 patients. The mean change was a significant increase of 35.4%

The BUN increased in 5, decreased in 4, and was unchanged in 2 patients. (Table II). The mean change was an increase of 5.1% which was not significant. Serum creatinine was reduced post-operatively in 6 patients and the mean change for all 11 patients was -7.6%. This represented an average decrease in serum creatinine from 1.56mg% to 1.37mg%. Urinary creatinine increased in 8 patients with a mean change of +40.8%. Average urinary creatinine per twenty-four hours was 1.30 Gm. prior to operation and 1.55 Gm. after the procedure. Urine volume increased

significantly after surgery with a mean change of +103.7%. Urine osmolarity was decreased in 7 patients with a mean change of -15.4% for all the patients.

The results of the ADH stimulation test showed that the urine osmolarity after operation was decreased in 7 and increased in one patient with a mean change of -12.5%. The increased water intake in the post-operative phase, along with the improvement in the glomerular filtration, is probably responsible for the reduction in urine osmolarity both in the twelve hour urine specimen and in the specimen following ADH stimulation. The PSP test, completed successfully on 3 patients, indicated no change after the operation on 2 patients (#3, 4) and a significant improvement in one patient (#5).

DISCUSSION

In the animal experiments it was observed that a sustained and significant decrease in urine output occurred during periods of increased intravesical pressure. This response was present in both kidneys and could be prolonged for 135 minutes. Release of bladder pressure was accompanied by an immediate return in urine output to the previous levels of the control period. No changes in blood pressure or urine osmolarity were associated with the bladder distention. Since urine osmolarity is a function of tubular reabsorption and the animals were subjected to maximum ADH stimulation throughout the experiment, it appears that the reduced urine output was not the result of increased tubular reabsorption. It is more probable that a reduction in glomerular filtration is responsible for the reflex oliguria present with bladder distention. The decreased creatinine clearance during periods of bladder distention is further evidence of the role of glomerular filtration rate (GFR) in the vesicorenal reflex.

It has been proposed that oliguria and reversible uremia may in part be due to bladder distention by means of a vesicorenal reflex. Increased intravesical pressure occurs in patients with prostatic obstruction.[4] Relief of obstruction has been followed in some instances by a remarkable improvement in renal function. The clinical studies on patients undergoing prostatectomy suggest that the GFR as measured by creatinine clearance was increased significantly following the operation.

This indicates a strong correlation between the experimental results and the clinical findings. Bladder distention with an elevated intravesical pressure is definitely associated with a reduced GFR and the release of bladder pressure is followed by a return of the GFR to normal.

The clinical study showed that the relief of lower tract obstruction is usually accompanied by an increase in glomerular filtration. The estimated GFR (64ml/min) prior to surgery in this series of 11 patients is very similar to the average GFR determined in another series of 60 elderly men with prostatic enlargement. It has been established that chronic obstruction to urine flow in the elderly prostatic patient leads to a reduction in GFR and renal blood flow (RBF) greater than that accounted by age alone. In one study of 12 patients examined before and after prostatectomy there was an increase in RBF but no significant change in GFR following surgery.[14] In another small study of 6 patients, it was concluded that tubular function, not GFR, was improved after relief of obstruction.[10] The results of this clinical investigation support the theory that GFR improves significantly after the relief of lower tract obstruction.

Since standard and comparable conditions of renal function were obtained by the use of urea-ADH diuresis, there is good evidence for accepting the presence of a vesicorenal reflex. No hydraulic connections between the bladder and the kidneys were present. Increased bladder pressure causes a decreased urine output

by some undetermined mechanism. It is likely that there are tension receptors within the wall of the bladder which initiate the afferent phase of the vesicorenal reflex. Repeated experimentation has shown that increased tension in the bladder, not in the ureters, produces the reflex. It appears related to a pressure phenomenon and is not influenced by the volume contained in the bladder. The tension receptors are stimulated not only in the presence of rapid bladder distention, but whenever there is increased intravesical pressure. The experimental results in dogs #3 and #6 showed that a positive response is obtained even with slow infusions simulating the urine output. Bladder pressures of 15 mm Hg. in the dog initiated the reflex and a further increase in pressure was correlated with a further decrease in urine output. Once the reflex is elicited, persistent bladder distention will maintain a sustained decrease in urine output for over two hours without fatigue of the tension receptor mechanism. In all the experiments release of bladder pressure was followed by a prompt recovery of urine output to previous levels. The reflex could be reproduced in the same dog several times and is further evidence for a tension receptor mechanism which is reversible and dependent on bladder distention.

Several investigators have proposed that a neurogenic pathway may be responsible for the vesicorenal reflex.[3, 8] It has been reported that the depression of urine output following bladder distention can be abolished by denervation of the renal artery.[20] These results were obtained in a dog preparation in which there

were no direct connections between the bladder and the kidneys. However, the method of denervation is not described and dissection of the renal artery or even complete denervation of the renal artery does not necessarily imply complete denervation of the affected kidney. Transection of the renal vessels, as well as dissection of the renal capsule, and then reanastomosis of the vessels results in complete denervation of the kidney. Renal autotransplantation was performed in three dogs four to six weeks prior to the experimental procedure to elicit the vesicorenal reflex. (See Table III). There was a significant reduction in urine output of the normal kidney (mean decrease of -27%) with increased intravesical pressure, but there was no significant effect on the urine output of the denervated kidney. Histologic sections of the autotransplanted kidneys involved in this set of experiments appeared normal. While an additional number of experiments are needed, it seems apparent that complete renal denervation can abolish the vesicorenal reflex.

Two other methods of investigation have been reported. Stimulation of both sectioned and intact nerves subserving bladder function has been performed in an attempt to elucidate the pathways of the vesicorenal reflex. It is difficult to interpret the results since any stimulus of sufficient intensity can produce a reflex oliguria. Despite some conflicting evidence, it has been proposed that the afferent pathway is via the pelvic nerves and the efferent one is via the splanchnic nerves.[3, 8] The use of pharmacologic agents offers a more promising method. It has been shown

that when adrenaline or serotonin were injected intravenously into dogs, the vesicorenal reflex was significantly enhanced.[20] On the other hand, when pilocarpine, hexamethonium, or histamine were administered, there was no significant effect on the reflex. The local application of tetracaine to the bladder mucosa also did not appear to inhibit the reflex. There was no control data, however, on the effect of adrenaline and serotonin on urine output without bladder distention which tends to invalidate these findings. Increased sympathetic tone due to circulating catecholamines might lead to a decreased urine output as a result of the decrease in RBF.

Since the autonomic nervous system is thought to be involved in the mediation of the vesicorenal reflex, a sympathetic blocking agent was given to see if the reflex could be abolished. Regitine, an adrenergic blocking agent, was used in one experiment in order to test this theory. It was found that Regitine did not appear to abolish the vesicorenal reflex. It was noted during sympathetic inhibition that bladder distention produced a sustained decrease in blood pressure together with a reduction in urine output with a return of both to previous levels upon release of bladder pressure. It is possible that the reflex affects the kidney selectively only because the normal sympathetic tone prevents the reduction of systemic blood pressure. Sympathetic blockade may inhibit this compensatory mechanism and bladder distention could then produce systemic hypotension. Further investigation on the effect of sympathetic tone and bladder distention is necessary.

Since the micturition reflex is mediated by the parasympathetic nervous system, it would be of interest to determine if the parasympathetic nervous system is involved in the vesicorenal reflex. It was found in one of our experiments that parasympathetic inhibition with Banthine did not abolish the response to bladder distention although a reduction in intravesical pressure was noted. Another study, however, has suggested that parasympathetic blockade abolishes the reflex.[12]

The possibility of the release of a humoral agent by the bladder should be considered. At the present time there is no evidence to support this theory. The reflex has been prolonged for over two hours, reproduced in the same dog several times in one experiment and does not effect the autotransplanted kidney. This evidence tends to mitigate against the presence of a humoral agent.

Recent experimental work has stressed the idea of a vesico-hypothalamic reflex which releases ADH.[20] This ADH is then believed to cause the reduced urine output associated with bladder distention. Our experimental method with the administration of large doses of exogenous ADH makes this theory untenable. A neurohumoral pathway may be responsible for the reflex oliguria, but release of ADH does not appear to be involved.

Finally, the receptor mechanism by which urine production is reduced in the kidney should be investigated. A reduction in glomerular filtration, an increase in tubular reabsorption, or a combination of these two functions could lower the

urine output. Increased tubular reabsorption secondary to ADH release is not responsible and the lack of significant changes in urine osmolarity during the experiment is additional evidence against alterations in tubular reabsorption during bladder distention. Variations in GFR is probably the cause of the reduced urine output which is supported by decreased creatinine clearance during periods of distention. One study has suggested that there is a reduced RBF with bladder distention.[20] While the reduction of total RBF leading to a lowering of GFR is a likely explanation, further evidence is necessary to establish this hypothesis.

SUMMARY

Our experimental results indicate a definite relationship between decreased urine output and bladder distention. This vesicorenal reflex is probably initiated by a tension receptor mechanism in the bladder wall. The pathways between the bladder and the kidneys are not well understood. While pharmacological blockade did not appear to alter the response, kidney denervation abolished the vesicorenal reflex. The receptor mechanism in the kidney is concerned probably with changes in GFR leading to a decreased urine output. The role of RBF in this vesicorenal reflex is very unclear. There may be a neurovascular response which alters renal perfusion to lower the GFR or a direct effect on glomerular vessels perhaps mediated by the juxtaglomerular apparatus. Clinical studies showing an improvement in GFR following relief of prostatic obstruction suggest that the vesicorenal reflex may have an important role in the reversible uremia associated with lower urinary tract obstruction.

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TABLE I

EFFECT OF BLADDER DISTENTION ON URINE FLOW IN DOGS

Dog #	Control cc/min	Experimental Period			Time min.	Bladder pressure mm Hg	Recovery cc/min	
		cc/min	% dec e/c	% dec c/r				
Ia	2.90	1.60	-45%	-30%	15	5	2.27	
Ib	2.27	1.40	-38%	-44%	15	35	2.27	
2a	4.10	2.60	-37%	-33%	5	5	3.90	
2b	3.90	1.70	-56%	-60%	5	70	4.20	
3a	1.89	1.75	-7%	-20%	10	35.5	2.19	No ADH
3b	3.75	3.10	-18%	-32%	35	22.0	4.56	
3c	4.10	2.90	-29%	-28%	59	22.2	4.00	
4a	2.50	1.50	-40%	-23%	8	28.8	1.94	
4b	2.85	2.43	-15%	-20%	15	29.0	3.05	No ADH
4c	3.28	1.41	-57%	-55%	28	38.9	3.13	
4d	3.25	1.58	-51%	-51%	21	20.0	3.20	
5a	3.15	2.68	-15%	-13%	25	38.0	3.09	
5b	3.96	3.43	-13%	-11%	26	80.1	3.84	
5c	3.38	3.19	-6%	-4%	41	67.4	3.33	
5d	3.91	3.58	-8%	-8%	20	78.8	3.92	
6a	5.47	4.16	-24%	-18%	135	32.2	5.08	
7a	1.77	1.31	-26%	-35%	30	19.5	2.05	
	Mean Change		-28.4%	-28.5%				

TABLE II

EFFECT OF PROSTATECTOMY ON GLOMERULAR FILTRATION RATE AND BLOOD URINARY NITROGEN

Patient	G.F.R. (ml./min) (Creatinine Clearance)			B.U.N. (mg %)		
	Before	After	Change%	Before	After	Change%
1	75	128	+71%	19	20	+5%
2	42	88	+109%	11	14	+36%
3	86	86	0%	15	9	-40%
4	66	79	+19%	13	13	0%
5	43	61	+30%	18	19	+6%
6	47	68	+45%	28	22	-21%
7	33	45	+36%	31	23	-26%
8	76	73	-4%	13	13	0%
9	79	160	+102 %	9	10	+11%
10	85	70	-18%	20	14	-30%
11	69	69	0%	14	30	+ 114%
Mean	64	84	+35.4%	17	17	+5%

TABLE III

EFFECT OF BLADDER DISTENTION ON URINE FLOW IN DOGS WITH RIGHT KIDNEY DENERVATION

		Control (cc/2 min)	Experimental % dec. e/c		Time min.	Bladder pressure	Recovery (cc/2 min)
			R. Kidney	L. Kidney			
A	#1	6.98	-14%	-26%	32	48	6.96
B	#1	3.57	- 6%	-25%	30	42	3.64
	#2	4.10	-2%	-20%	24	52	4.18
	#3	4.83	+5%	-24%	30	52	5.00
C	#1	3.34	-4%	-38%	14	57	3.78
	#2	4.60	-4%	-26%	26	44	4.52
	#3	5.46	-5%	-29%	20	36	5.43
		Mean	-4%	-27%			

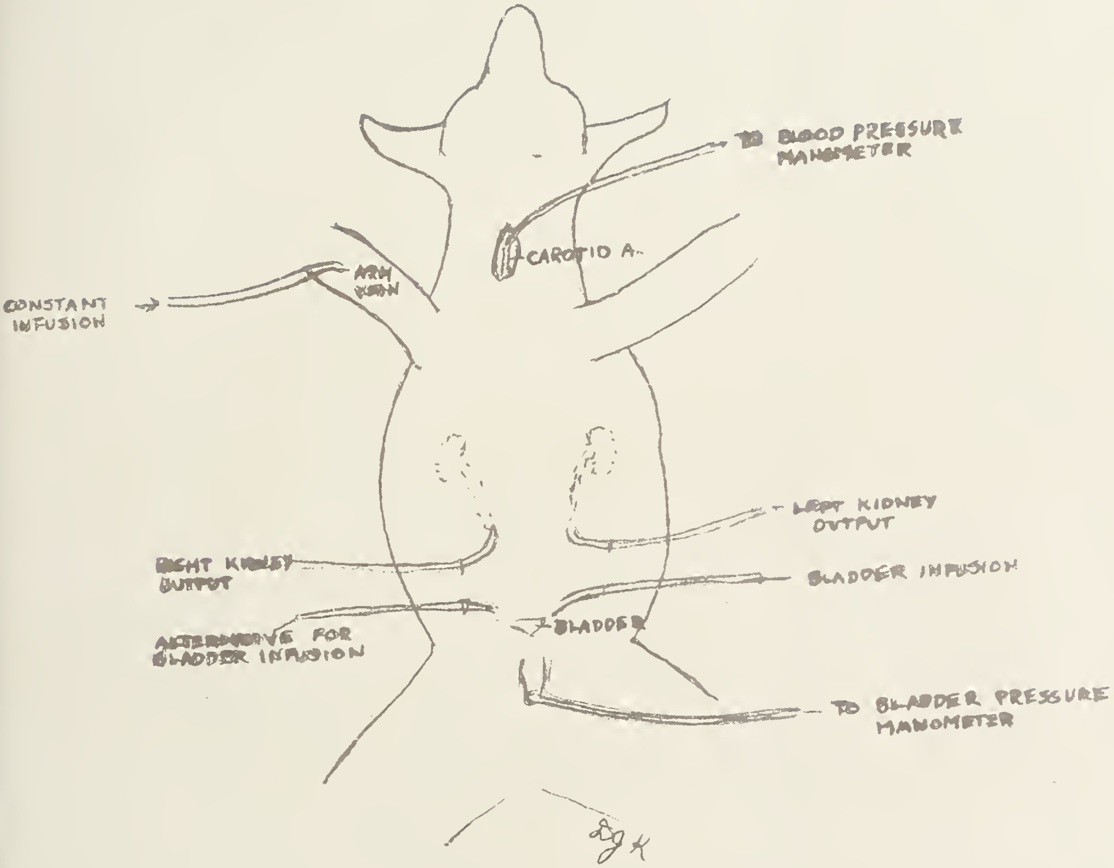
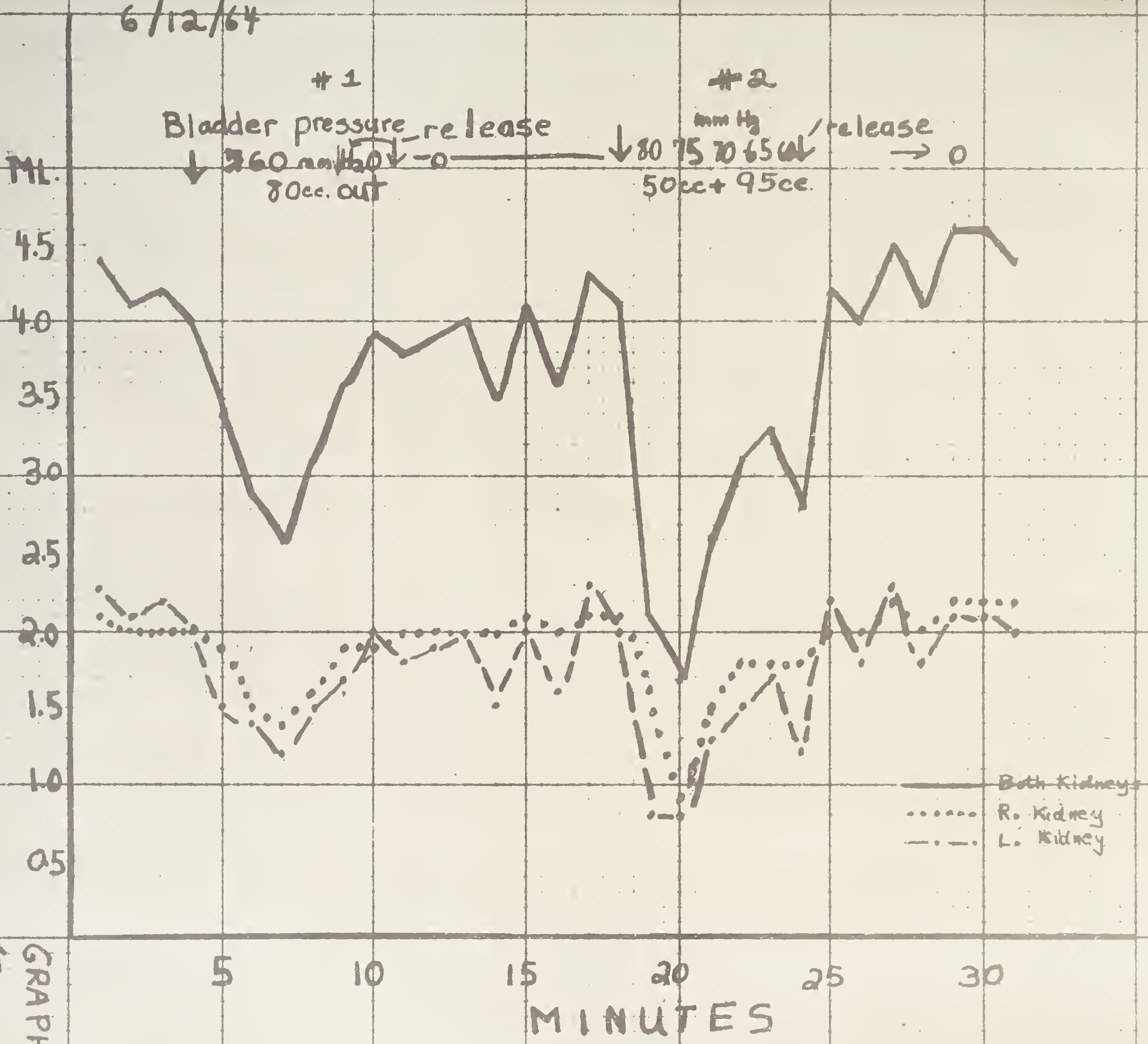
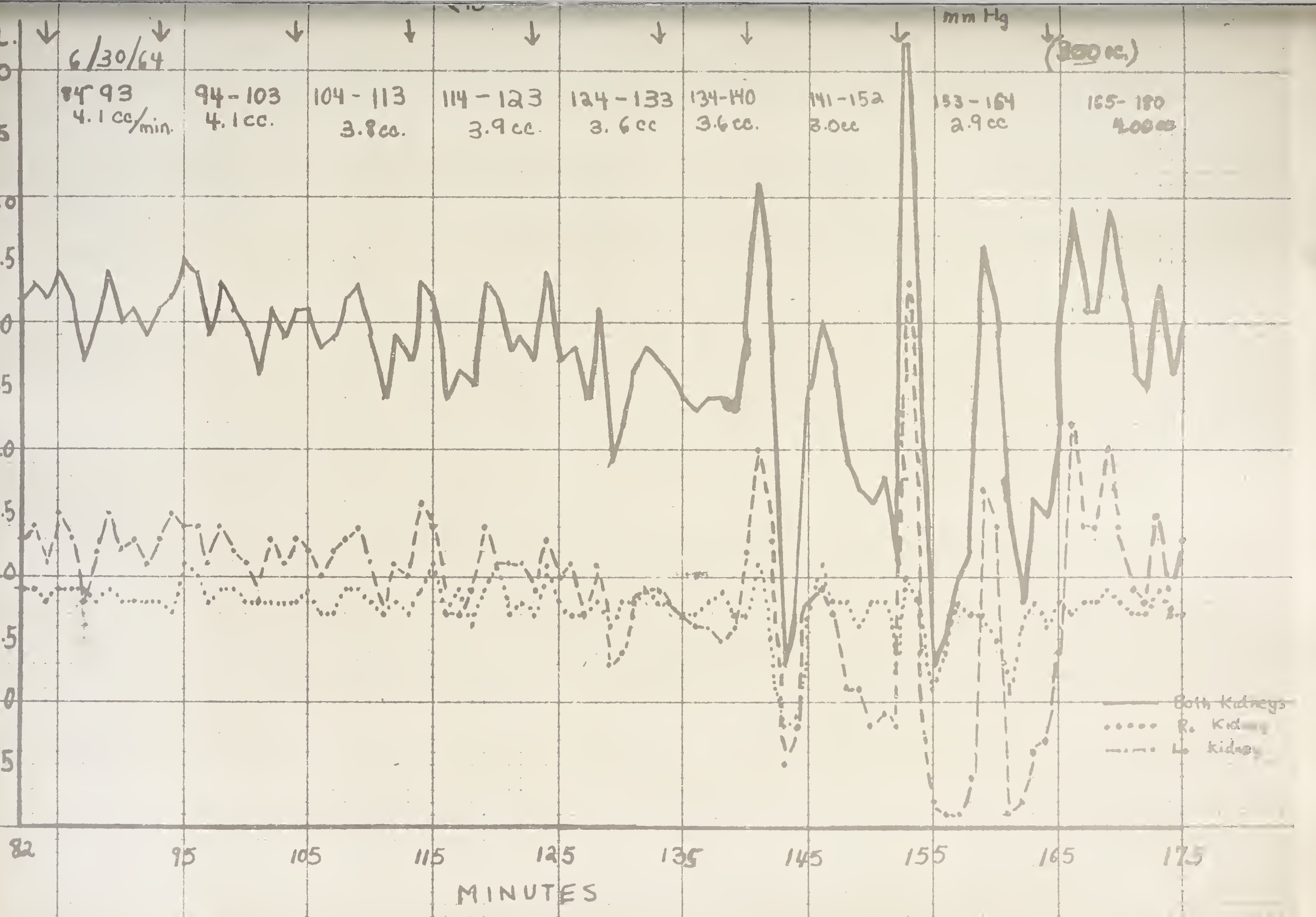


Fig. 1: ARRANGEMENT OF APPARATUS FOR ANIMAL EXPERIMENT

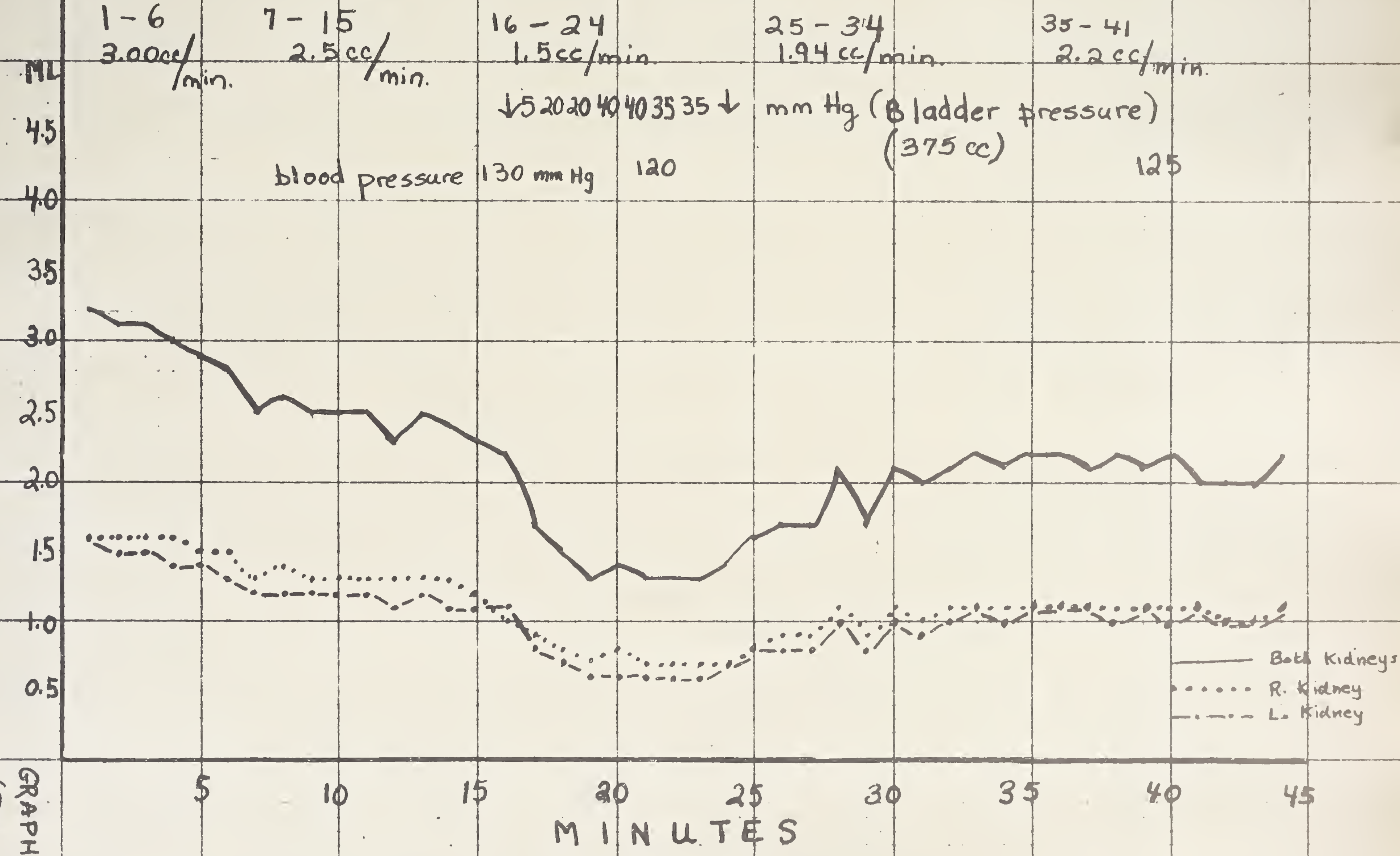


GRAPH I
(Expt. 2a + 2b)


ML.
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
6/30/64
84 93
4.1 cc/min.
94-103
4.1cc.
104 - 113
3.8cc.
114 - 123
3.9cc.
124 - 133
3.6cc
134-140
3.6cc.
141-152
3.0cc
153 - 164
2.9cc
165- 180
4.0cc
mm Hg
(300 cc.)
Both Kidneys
R. Kidney
L. Kidney
82
95
105
115
125
135
145
155
165
175
MINUTES

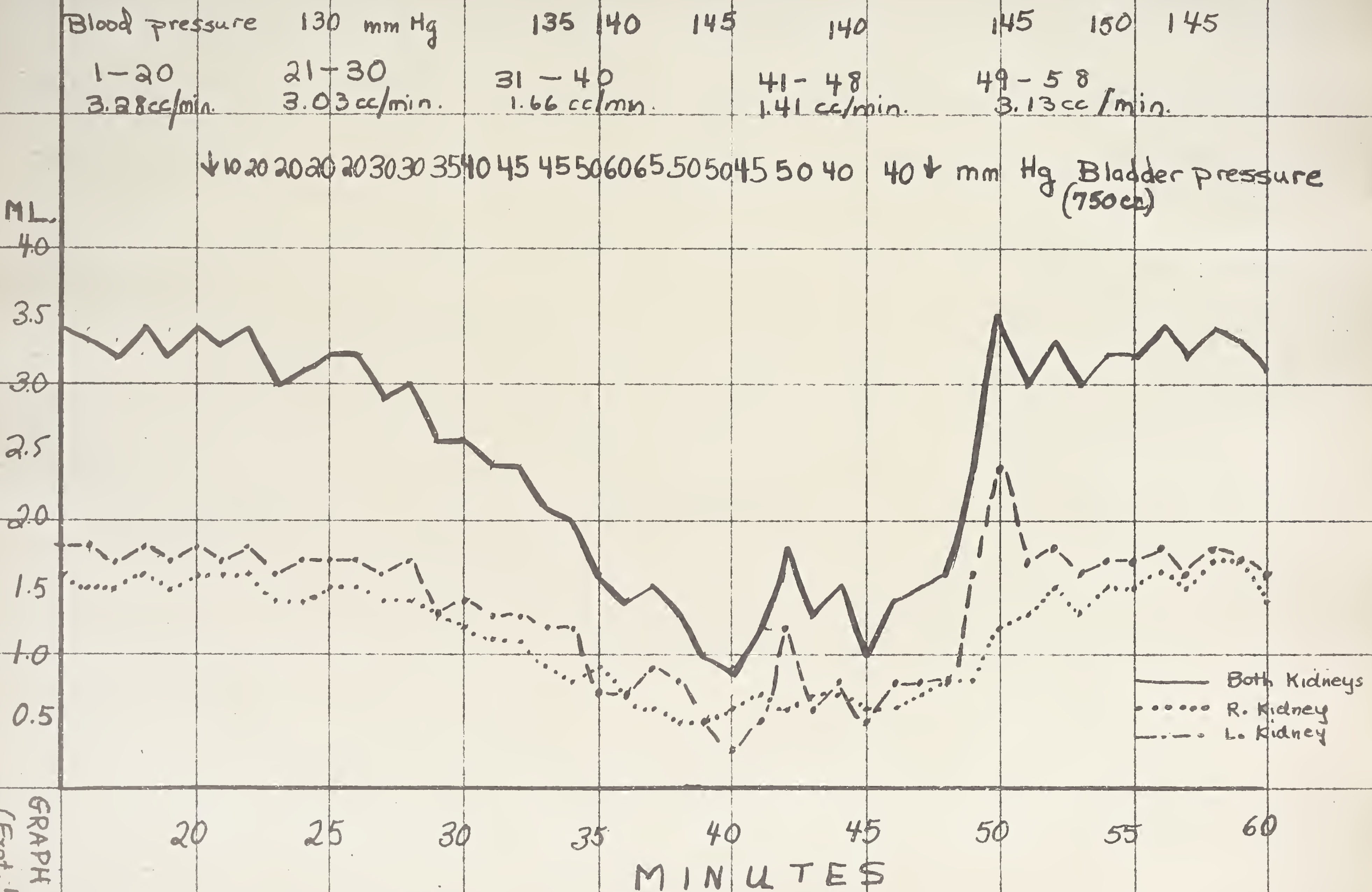
GRAPH II

7h/64

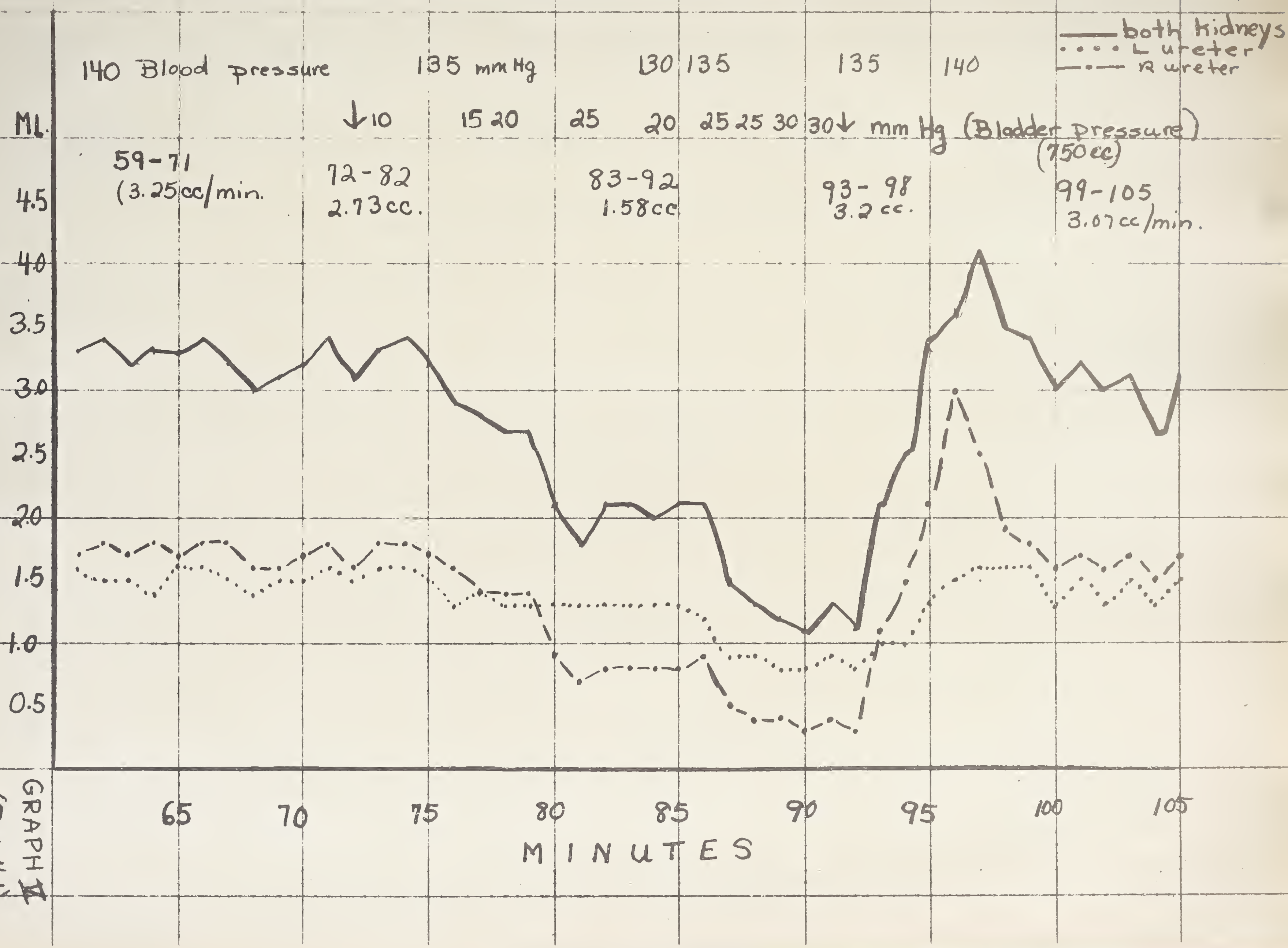


GRAPH III
(Expt. 4a)

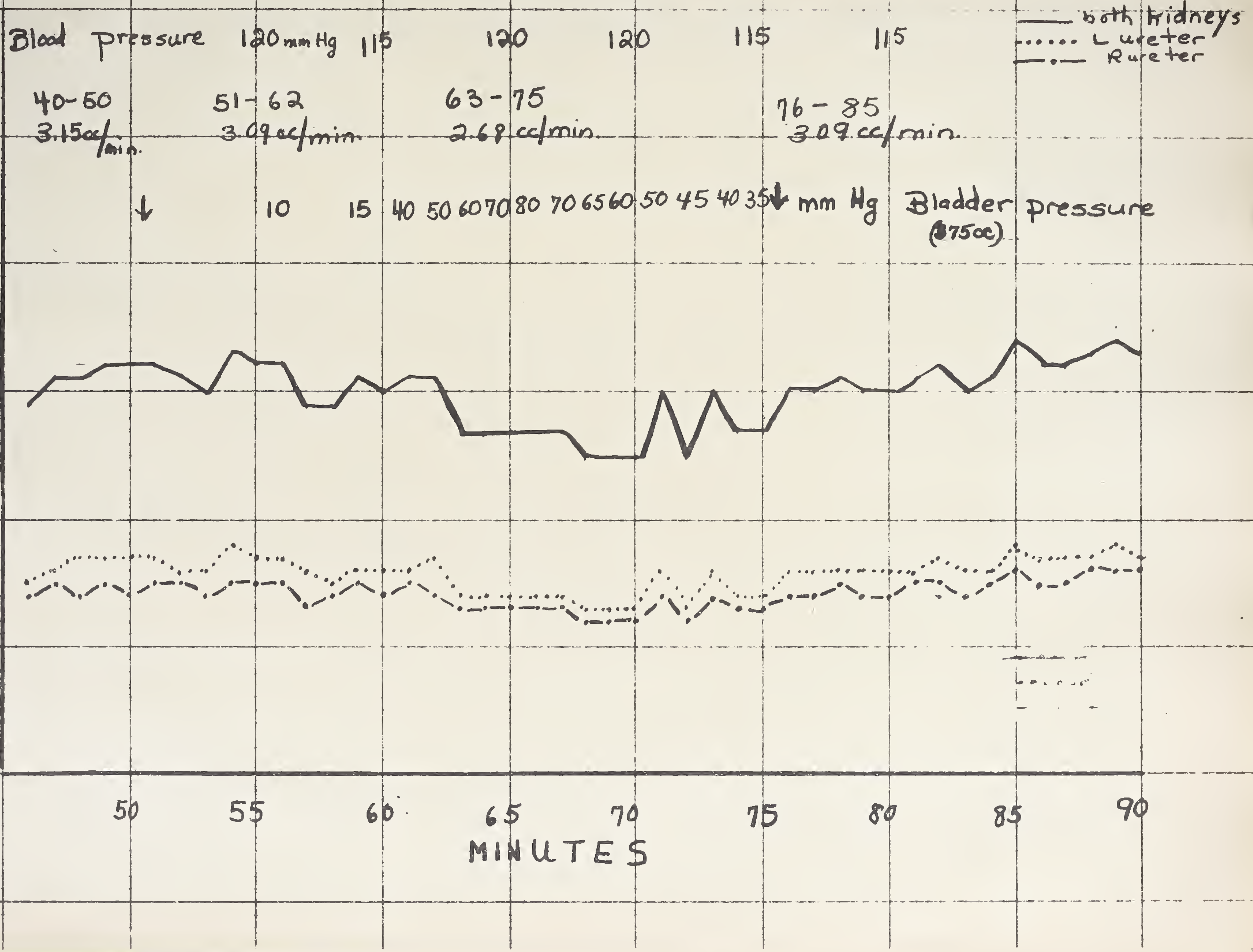
7/7/64



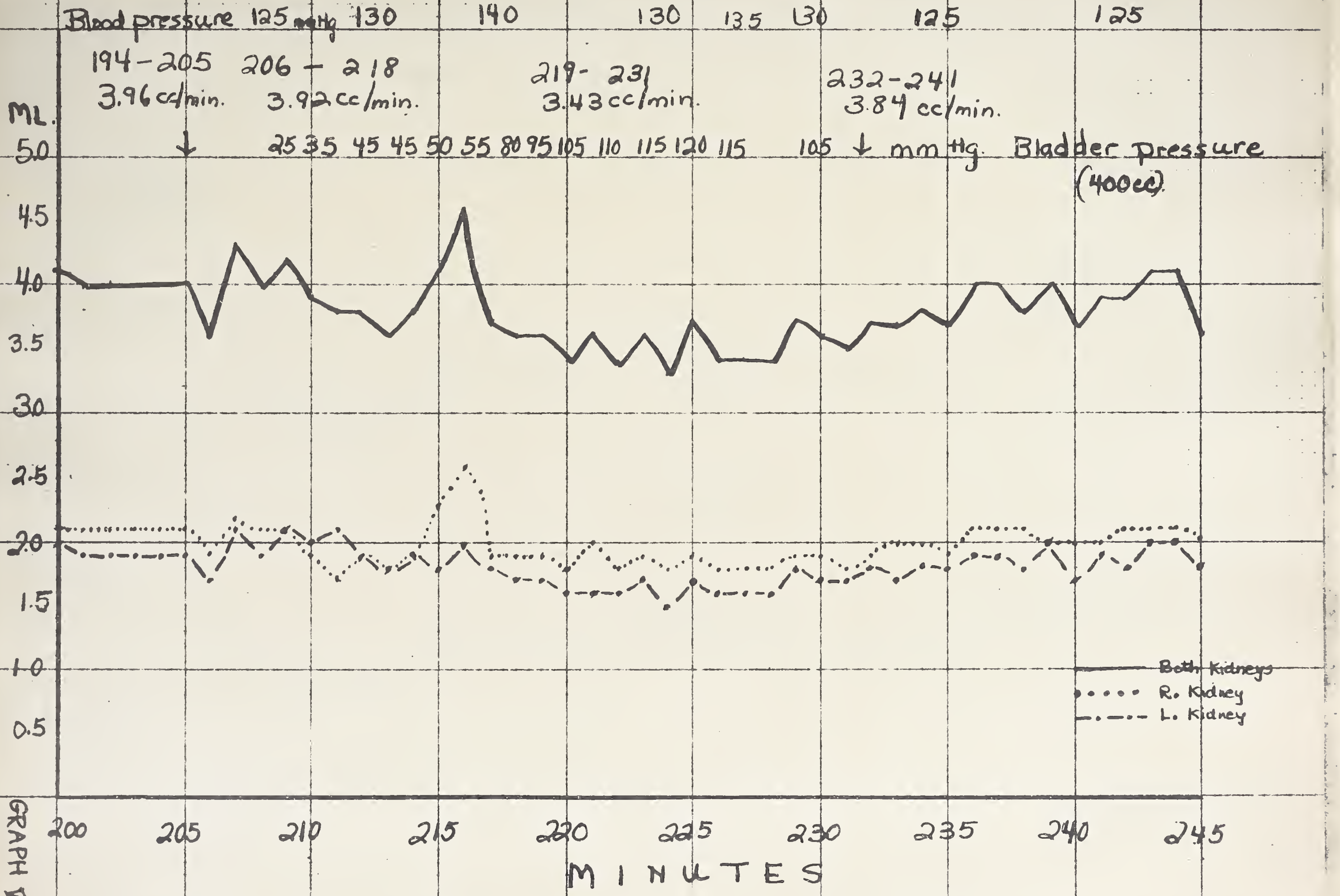
GRAPH IV
(Expt. 40)



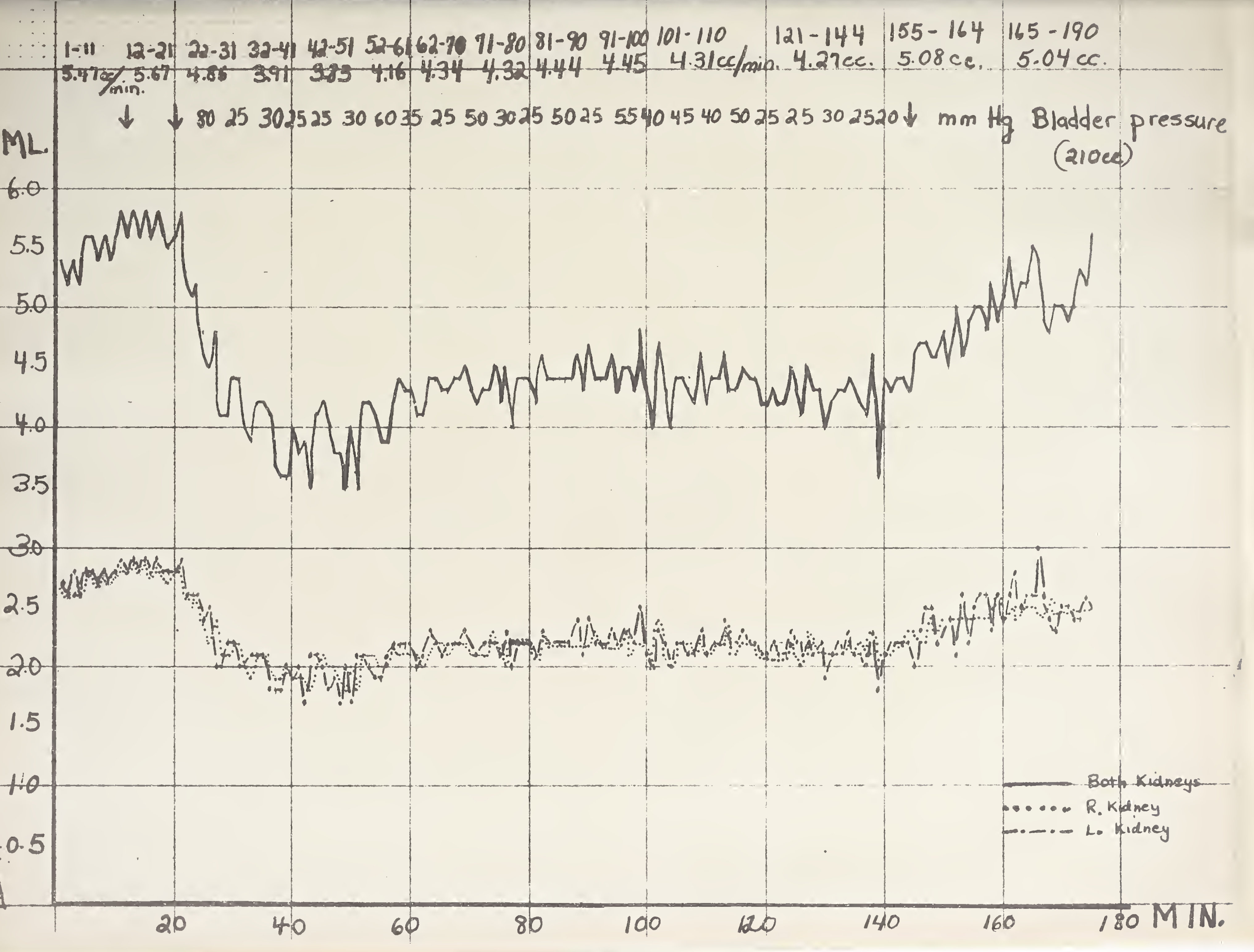
GRAPH X
(Expt. 4d)



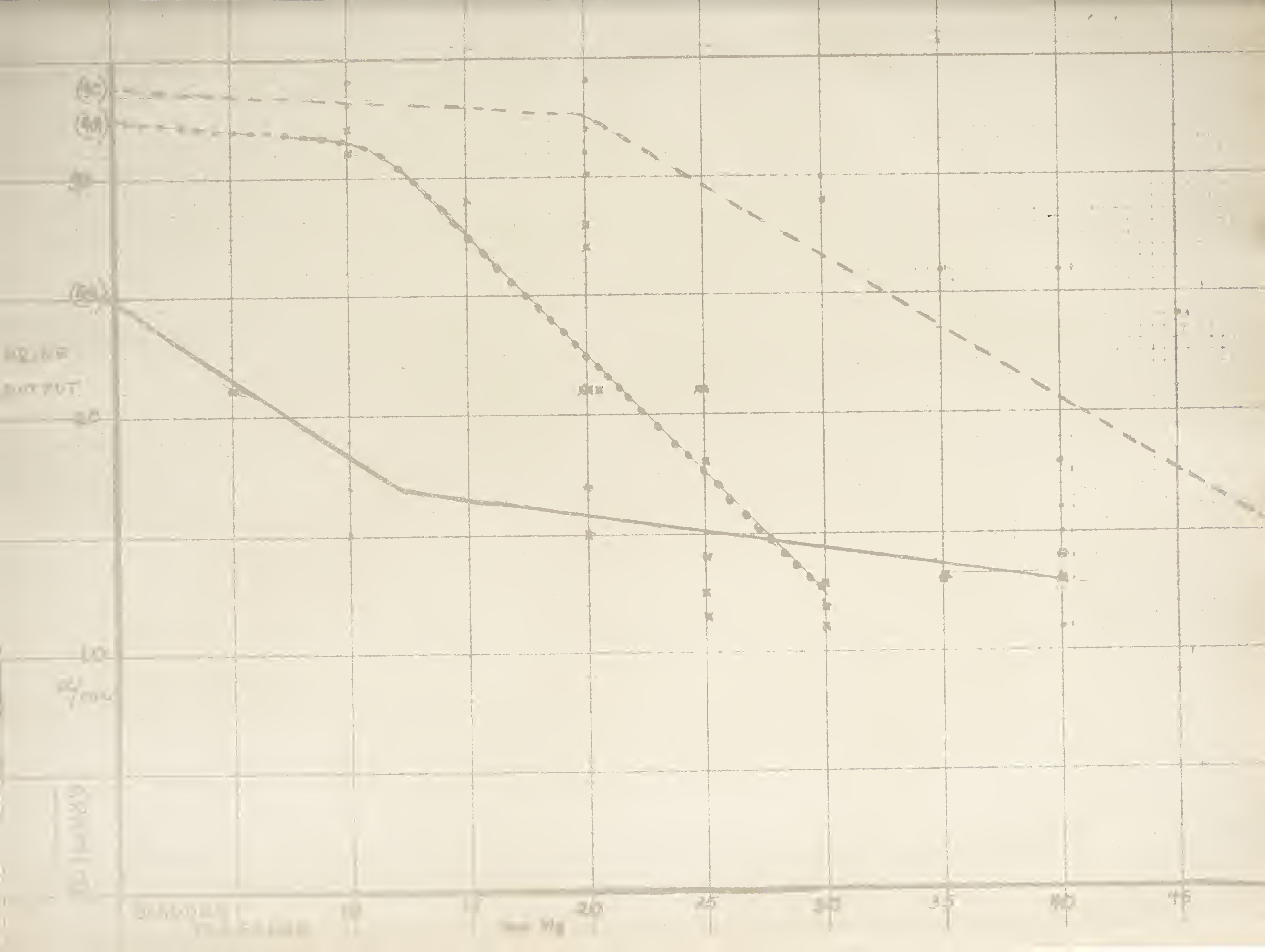
GRAPH VI
(Expt. 5a)



GRAPH VII
(Expt. 5c)


1-11 12-21 22-31 32-41 42-51 52-61 62-70 71-80 81-90 91-100 101-110 121-144 155-164 165-190
5.47cc/min. 5.67 4.86 3.91 3.83 4.16 4.34 4.32 4.44 4.45 4.31cc/min. 4.27cc. 5.08cc. 5.04cc.
↓ ↓ 80 25 30 25 25 30 60 35 25 50 30 25 50 25 55 40 45 40 50 25 25 30 25 20 ↓ mm Hg Bladder pressure (210cc)
ML.
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
20
40
60
80
100
120
140
160
180
MIN.
Both Kidneys
R. Kidney
L. Kidney

GRAPH VIII


OUTPUT
1.0
10
15
20
25
30
35
40
45
mm Hg
GRAPH

NAME AND ADDRESS | DATE

N. Burgess Record, Jr.
3 Sylvan Ave.

1/10/65