THE MECHANISMS OF INTRARENAL HEMODYNAMIC CHANGES FOLLOWING ACUTE ARTERIAL OCCLUSION

FEDERAL AVIATION AGENCY
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2. Renal Ischemia
3. Renal Hypoxia
4. Renal Arterial Occlusion
5. The Kidney and Vascular Resistances
6. The Kidney as a Secretor of Constrictors and Dilators
7. Renal Stress

The hemodynamic response of the kidney to acute arterial occlusion is poorly understood. The purpose of the present study was to determine intrarenal hemodynamic changes in intact and isolated kidneys following arterial occlusion. The relative roles of metabolic, myogenic and tissue pressure influences on the post-occlusion response were evaluated. The response of the kidney to occlusion was found to be complex depending on the interaction of a variety of physical and humoral forces. Increases in renal resistance appeared to be due in part to adrenergic agents and were enhanced by extending time of occlusion and lowering

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the arterial pressure. The combined effects of pre-venous dilatation and diminished tissue pressure resulted in a decreased resistance following shorter periods of occlusion. Pre-venous dilatation was accounted for by depressed vascular sensitivity to pressor agents and the presence of vasodilator substances. Changes in venous segment resistance were found to be of primary importance in both the autoregulatory phenomenon and the post-occlusion hyperemic response to short (fifteen second) occlusion periods.

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FOREWORD

It has been well documented for almost a half century that a prolonged period of systemic hypotension can lead to irreversible renal damage. The kidney appears to be unique in its high degree of susceptibility to injury during conditions of stress in which renal blood flow is depressed by the direct effects of hypotension or renal vasoconstriction. There are numerous reports of death from uremia following an apparent recovery from a period of sustained hypotension. As a logical extension of these previous reports it becomes of crucial importance to determine renal effects of stresses lesser in magnitude than shock itself, and evaluate their influences on human efficiency and well-being. It is probable that as man extends his contacts with high altitudes, the risk of encountering abnormal environmental conditions will be accelerated. It would be of particular interest to evaluate the effects of stresses which may be increasingly encountered in aviation, such as acute hypoxia and explosive decompression. The kidney would appear to be a logical "target organ" in these forms of stresses, and it is probable that both physical and neurohumoral factors are involved. The question as to the degree of temporary or permanent damage to the kidney under stress conditions is complex. The present study provides one answer to this question by undertaking an analysis of phenomena operating following temporary renal vascular occlusion.

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ABSTRACT

The hemodynamic response of the kidney to acute arterial occlusion is poorly understood. The purpose of the present study was to determine intrarenal hemodynamic changes in intact and isolated kidneys following arterial occlusion. The relative roles of metabolic, myogenic and tissue pressure influences on the post-occlusion response were evaluated. The response of the kidney to occlusion was found to be complex depending on the interaction of a variety of physical and humoral forces. Increases in renal resistance appeared to be due in part to adrenergic agents and were enhanced by extending time of occlusion and lowering the arterial pressure. The combined effects of pre-venous dilatation and diminished tissue pressure resulted in a decreased resistance following shorter periods of occlusion. Pre-venous dilatation was accounted for by depressed vascular sensitivity to pressor agents and the presence of vasodilator substances. Changes in venous segment resistance were found to be of primary importance in both the autoregulatory phenomenon and the post-occlusion hyperemic response to short (fifteen second) occlusion periods.

The hemodynamic response of the kidney following acute periods of renal artery occlusion is not clear in that both ischemic and hyperemic responses have been reported (1-3). Severe ischemia (4, 5) and marked hyperemia (6) have been found following acute periods of occlusion. It is generally conceded however, that reactive hyperemia as commonly observed in other tissues (7-21) is not found in the kidney (2, 22). The purpose of the present study was to investigate the post-occlusion hemodynamic responses of intact and isolated perfused kidneys with particular references to changes occurring in pre-venous and venous segment resistances. Experiments were carried out to determine the fundamental mechanisms responsible for post-occlusion renal ischemia and hyperemia. Studies were confined to total renal artery occlusion in dogs. Results indicate that the vascular response of the kidney to acute renal arterial occlusion is complex, a variety of factors operating to produce varying degrees of reactive hyperemia or ischemia depending on the net predominating forces.

METHODS

Experiments were carried out on intact innervated or denervated kidneys, and isolated kidneys perfused with heparinized homologous blood at constant blood flow or constant renal artery pressure from a dog or heart-lung preparation. Details of the experimental preparations have been previously described (23-28). Pressure-flow determinations were carried out in each experiment before and after total renal artery occlusion periods ranging from fifteen seconds to thirty minutes. Total resistance, pre-venous and venous segment resistance calculations were carried out in most experiments. Renal artery pressure, deep intrarenal venous pressure, urine flow and kidney weight were continuously measured and registered on a Sanborn direct writing recorder as previously described (23-28). Renal blood flow was either maintained constant by means of a properly occlusive Sigmamotor pump, or allowed to vary in experiments carried out at constant renal artery pressure (Starling shunt device) and measured with cylinder and stopwatch. In the series of *in situ* experiments, kidneys were studied in the innervated state or were denervated by a combination of both surgical procedures (complete isolation of renal pedicle) and chemical means (1% procaine, saturated gauze in contact with renal pedicle). Renal venous outflow was measured with cylinder and stopwatch follow-

ing direct cannulation of the renal vein, as previously described (23). A series of hypothermic experiments was also included in which renal vein blood temperatures were decreased to 10-14°C by means of a controlled water bath. The following drugs were used in certain experiments: Synthetic epinephrine (Winthrop Laboratories); norepinephrine (Levophed, Winthrop Laboratories); angiotensin II (Hypertensin, CIBA); histamine (histamine acid phosphate, Lilly). The following adrenergic-blocking agents were used in some experiments: phenoxybenzamine (Dibenzyline*) and phentolamine (Regitine, CIBA). The antihistaminic agent, diphenhydramine (Benadryl*) was also used.

A decrease in vascular resistance following arterial occlusion, when observed in the present study was designated RH (reactive hyperemia) while an increase in resistance was termed RI ("reactive ischemia") for ease in presentation. The dilator response of renal vessels to dilator agents was designated "active vasodilatation" in contrast to "passive dilatation" due to extra- or intravascular pressure changes. Renal blood flows in intact kidneys averaged 3.0 cc./min./gm. kidney weight (range, 2.0-4.1) at an average renal artery pressure of 148 mm. Hg. Renal blood flows in isolated perfused kidneys averaged 2.8 cc./min./gm. kidney weight (range, 1.3-5.5) at an average renal artery pressure of 130 mm. Hg.

RESULTS

Results are divided into three main areas for special consideration: (a) the characteristics of the renal hemodynamic responses to arterial occlusion; (b) the mechanisms responsible for the various changes in renal hemodynamics following arterial occlusion, and (c) a comparison of the segmental resistance characteristics of autoregulation and post-occlusion reactive hyperemia.

The characteristics of the renal hemodynamic responses to arterial occlusion. An initial series of six experiments was carried out on the heart-lung perfused kidney to characterize the renal vascular response to renal artery occlusion. Renal artery pressure was maintained constant between 90 to 165 mm. Hg. The renal arterial inflow tubing was cross-clamped for periods ranging between thirty seconds and twenty minutes. It was observed that an overshoot in renal blood flow (RH) occurred during the post-occlusion period in four kidneys. Reactive hyperemia persisted for three to twelve minutes following occlusion periods between thirty seconds and twenty minutes. Two kidneys, however, exhibited marked post-occlusion decreases in renal blood flow (RI) lasting up to fifteen minutes with occlusion periods between eight and ten minutes.

Since these initial observations clearly showed two opposite types of responses with apparently identical experimental conditions, additional experiments were designed to further characterize the responses. Six experiments were undertaken to compare the effects of arterial occlusion in a kidney both in the intact (*in situ*) and isolated, perfused states. Figure 1 shows data from a single experiment. It is seen that a depressed renal blood flow occurring in the intact kidney is not observed in the isolated state following a five minute period of occlusion.

It was incidentally noted in the initial experiments that the type of post-occlusion response was influenced by the length of occlusion. Experiments on seventeen kidneys were therefore carried out to explore the relationship of time of occlusion to the post-occlusion response. Figure 2A illustrates the influence of time of occlusion in intact and isolated perfused kidneys. It is seen that a five minute period of arterial occlusion results in RH in both organs whereas a twenty to thirty minute period produces marked RI in each kidney. Figure 2B presents raw and calculated data from one isolated kidney experiment. It is observed that as time of occlusion is increased, the degree of RH increases but as time is further extended, a definite period of RI is noted. Table I summarizes results from seventeen kidneys and in general shows that although intact kidneys more readily exhibit RI following shorter periods of occlusion (fifteen seconds to five minutes), most intact and isolated organs show RI following longer periods of occlusion (six to twenty minutes).

*Appreciation is expressed to Smith Kline & French for the generous supply of Dibenzyline, and to Parke, Davis & Company for the donation of Benadryl.

Since experiments had shown time of occlusion an important variable in the vascular response to occlusion, the question arose as to the effects of a repeated series of occlusions of equal time. It was found that when RI was observed following a given time of arterial occlusion, repetitive occlusions of the same time period sucessively drove resistance to higher values. This finding is illustrated in Fig. 3 in a perfused kidney and is also suggested in Fig. 1. This relationship was observed in seven kidneys in both isolated and intact denervated states. The duration of RI was persistent in a given post-occlusion period, lasting from fifteen minutes to two hours.

Results from a preliminary experiment suggested that the level of the renal artery pressure had an influence on the vascular response to occlusion. A series of nine isolated perfused kidney experiments was therefore carried out to explore this relationship. Periods of occlusion ranged from three to five minutes. Table II shows that RH is ordinarily observed in the renal autoregulatory range (100-125 mm. Hg). In contrast, mean values show RH to be replaced by RI at arterial pressures below the autoregulatory range (45-80 mm. Hg). In individual experiments, RH was not always replaced by RI at lower renal artery pressures but the degree of RH was less. Figure 4 shows data from a single kidney experiment and indicates that the degree of RH increases as a function of increased renal artery pressure.

Mechanisms responsible for the various changes in renal hemodynamics following arterial occlusion. As a natural extension of the previous findings, a second group of experiments was undertaken to explore the various possible factors responsible for changes in renal vascular resistance following arterial occlusion. These experiments are divided into two groups: factors responsible for (a) reactive hyperemia (RH) and (b) reactive ischemia (RI).

(a) *Mechanisms of the post-occlusion hyperemic response.* Previous experiments in this investigation suggested that both changes in tissue pressure and active vasodilatation appeared to have a role in producing the RH response. It was therefore decided to systematically evaluate the relative roles of the venous and pre-venous segment resistances in the hyperemic response to arterial occlusion. It has been previously shown (24,25) that venous segment resistances in the kidney are passive reflections of tissue pressure and weight. This was verified in the present study when tissue pressure, deep venous pressure and weight changes were simultaneously recorded. The first series of experiments designed to evaluate the roles of segmental resistances was carried out on twelve heart-lung perfused kidneys. Experiments were separately executed at constant arterial inflow and constant renal artery pressure for purposes of comparison. Results during the post-occlusion period were observed to fall into one of two categories: (a) a predominate decrease in venous segment resistance (effect of diminished tissue pressure), and (b) combined decreases in both prevenous and venous segment resistances, indicating both active and passive components of resistance. Figure 5A shows mean resistance values from twelve experiments on seven kidneys. Post-occlusion segmental and total resistance values are shown following a three minute arterial occlusion period. The lowest average drop in total resistance is shown and three recovery points are also indicated. The period of recovery to control values ranged from three to ten minutes. Results show that the drop in total resistance (R_t) is primarily accounted for by a decrease in venous segment resistance (R_v), i.e., by a diminished tissue pressure. Changes in deep venous pressure, kidney weight and total resistance were found to closely follow one another. Decreases in kidney weight were closely correlated with decreases in venous segment resistance, and the recovery of kidney weight corresponded closely with the restoration of resistances to control values (see Figs. 5B and 4). Figure 5B shows mean values in segmental and total resistances in thirteen experiments (five kidneys). Results demonstrate a fall in total resistance following an average occlusion time of four minutes. The decrease in R_t is due to the combined effects of venous and prevenous segment resistances. Results from experiments shown in figures 5A and 5B indicate that reactive hyperemia may be accounted for on the basis of passive, or active and passive changes in resistance.

Attempts were made to remove by experimental means the active vasodilatation component(s) in the post-occlusion response. A

series of hypothermic experiments on the heart-lung perfused kidney was carried out for this purpose. Control experiments for each study were done first at normal temperatures and were then executed at blood temperatures from 10 to 14°C. At the lower temperatures the dilatation response of the kidney to intra-arterial injections of histamine was virually abolished, whereas a marked vasodilatation to histamine was regularly observed in the normothermic state. It is seen in Figure 6A (five kidneys) that RH is obtained in the normothermic state, and is accounted for by decreases in both pre-venous and venous segment resistances. On the other hand, under conditions of hypothermia, RH is again observed but is accounted for on the basis of a marked decrease in venous segment resistance. Figure 6B shows raw data and resistance calculations for one experiment. Results from this group of experiments indicate that the primary factors producing RH are pre-venous segment dilatation and a decrease in venous segment resistance due to diminished tissue pressure.

The antihistaminic agent, phenylhydramine (Benadryl), 10 mg./kg. body weight, was introduced into the blood of three dog-pump kidney preparations after obtaining a control post-occlusion response with Dibenzyline (Table III). If histamine was released during the period of occlusion, the post-occlusion response after Benadryl did not completely confirm the presence of a histamine-like substance.

It was considered a possibility that the effects of arterial occlusion might enhance the vascular responsiveness of the pre-venous segment to circulating pressor agents. This effect would result in the presence of RI on the basis of an enhanced constriction response. A series of ten dog-pump kidney perfusion experiments was carried out at constant arterial inflow to explore this possibility. Occlusion periods were five to fifteen minutes, and intra-arterial injections of 0.04 to 0.3 micrograms of epinephrine and angiotensin were given during the pre- and post-occlusion periods. Injections were made during constant flow perfusion so that changes in arterial pressure were indicative of alterations in resistance. Flows were adjusted so that pre- and post-occlusion renal artery pressures were equal at time of drug injection. Amounts of drugs injected were adjusted to the flow rate so that similar concentrations would reach the organ. Results are seen in Figure 7 (six kidneys) and show a depressed vascular responsiveness during the post-occlusion period to both epinephrine and angiotensin. Depressed responses were evident when as much as four times the pre-occlusion doses were injected.

It was recognized early in the course of the investigation that a drop in transmural pressure occurring during the occlusion period might explain the presence of reactive hyperemia on the basis of a myogenic response. This possibility was explored by attempting to exclude or diminish the complicating dilator effects of accumulating metabolites: occlusion periods were reduced to fifteen seconds and the results from seven heart-lung kidney experiments are shown in Fig. 8. Reactive hyperemia was observed in all experiments, however, the drop in total resistance was accounted for by a fall in venous segment resistance. Changes in kidney weight and deep venous pressure were closely correlated during the post-occlusion period. Since pre-venous segment resistance remained constant in individual experiments, the role of a myogenic response in the reactive hyperemia phenomenon appears to be excluded.

(b) *Mechanism of the post-occlusion ischemic response.* The above experiments were designed to determine the mechanism of reactive hyperemia in the kidney. A major problem still remained in gaining an understanding of the underlying mechanisms of the post-occlusion ischemic response occurring in kidneys under the previously described conditions under (a) above. Experiments were therefore designed to attack this problem. In the first group of studies, leg or kidney artery supplies were established in series with a heart-lung perfused kidney, and were placed a short distance downstream from the organ to be subjected to arterial occlusion. Six experiments were carried out and results were entirely negative. No evidence was obtained for the presence of vasoactive agents released into the venous effluent of the test organ or formed in the blood. Interestingly however, it was noted that a vasoconstrictor agent was released from the kidney immediately following transfer to the isolated perfused state. This agent had an

adrenergic-like action on the down-stream assay organ. It appeared to be derived from the tissue of the test kidney since the vascular bed of the latter had been thoroughly flushed with blood from the heart-lung system prior to transfer, the effluent blood being discarded. It was considered possible that pressor agents might be released from a kidney during the occlusion period in concentrations small enough not to affect an assay organ. A series of ten experiments was carried out utilizing the adrenergic blocking agents phenoxybenzamine and phentolamine. Experiments were executed on the dog-perfused kidney and the *in situ* organ in which RH is more readily obtained following shorter occlusion periods. The results are of interest from several standpoints. Phenoxybenzamine or phentolamine reversed the increase in vascular resistance during the post-occlusion period in eight of the ten experiments (Table III). In seven experiments in which phenoxybenzamine was given twenty to seventy minutes prior to arterial occlusion, the RH response was modified in that only a temporary ischemic period occurred. Figure 9 shows the results from a single experiment following administration of phenoxybenzamine. The increase in resistance is less in degree than pre-phenoxybenzamine and of a temporary nature. These data suggest that adrenergic-like agents are most probably involved in producing the post-occlusion increase in resistance. The formation of angiotensin may account in part for findings in which adrenergic blocking agents were unsuccessful, and in those in which a temporary post-occlusion elevation in resistance was observed.

As a final point of consideration, it can be seen from the post-occlusion arterial pressure records that there is an early transient rise in total resistance beginning from two to eight seconds post-occlusion and persisting from fifteen to fifty seconds. Although this response was only fleeting, its regular appearance is of interest. From an analysis of the data, this early transient increase in resistance can be characterized as follows: (a) it occurs in the pre-venous segment (Fig. 2B); (b) it may diminish in magnitude or disappear as the time of occlusion is increased (Fig. 2B); (c) it disappears in the hypothermic state (Fig. 6B); (d) it is not abolished by adrenergic blocking drugs; (e) it may disappear at arterial pressures in the hypotensive range; and (f) it occurs only after a given filling of the vascular bed has been achieved (Fig. 2B). This response appears to meet the characteristic criteria of a myogenic (Bayliss') phenomenon.

(c) *A comparison of the segmental resistance characteristics of autoregulation and post-occlusion reactive hyperemia.* Several possible mechanisms responsible for the development of post-occlusion reactive hyperemia have been discussed in the previous section (a) above. It was considered of interest to contrast the changes in pre-venous, venous and total vascular resistances in the same kidneys during autoregulation and reactive hyperemia to determine if a common underlying mechanism might account for the two phenomena. Experiments were carried out on fifteen heart-lung perfused kidneys and results are presented in Fig. 10. Pressure-flow-resistance values for each kidney were determined prior to and immediately following arterial occlusion periods averaging three minutes. The major similarities between the autoregulation phenomenon and reactive hyperemia are (a) decrease in venous segment resistance coincident with decrease in total resistance; (b) close correlations of kidney weight, deep venous pressure, venous segment resistance and total resistance during the post-occlusion period and following an elevation of renal artery pressure. Although the pre-venous segment resistance appears to play a greater role in the post-occlusion hyperemic response than in the autoregulation phenomenon, this would not be the case if shorter occlusion periods were chosen as seen in Fig. 8.

DISCUSSION

An important aim of the present study was to describe the conditions under which a decrease in resistance (reactive hyperemia) or an increase in resistance (reactive ischemia) may occur following a period of acute renal artery occlusion (fifteen seconds to thirty minutes). It was found that the two chief variables influencing the type of response are time of occlusion and the post-occlusion arterial pressure. The renal nerves were excluded

from having a significant role in the phenomena. The only difference in response between isolated and intact kidneys appeared to be that a longer time of occlusion was required in the isolated perfused kidney to produce the same degree of ischemia as that ordinarily observed in the intact innervated or denervated organ.

A second aim of the investigation was to determine the mechanisms underlying the post-occlusion renal vascular response. Figure 11 is a schema, presented to illustrate the various possible components involved in the post-occlusion hyperemic and ischemic responses observed in this study. Results indicate that the renal vascular response to arterial occlusion is complex, involving a variety of opposing forces. These forces or influences are expressed in varying degrees depending on the conditions of the experiment as illustrated by the results of this investigation.

The post-occlusion hyperemic response is more readily obtained with arterial perfusion pressures in the autoregulatory range, and following relatively short occlusions. A decrease in total resistance is observed following a fifteen second occlusion which is accounted for on the basis of changes in venous segment resistance. Schmid and Spencer (6) have recently reported similar decreases in resistance following short occlusions in the in situ kidney. Results from the present study indicate that a decrease in tissue pressure is the primary underlying mechanism accounting for the hyperemic response to short (fifteen second) occlusions, and to the drop in total resistance when arterial pressure is decreased through the autoregulatory range. The role of tissue pressure in the autoregulation phenomenon has been previously described (24, 25, 27). Despite the post-occlusion period good correlations were observed between changes in kidney weight, tissue pressure (unpublished data), deep venous pressure, venous segment resistance and total resistance. There is evidence from the present study that a myogenic mechanism (7) is not operative in the hyperemic response in the kidney although it may be involved in other organs (10, 12, 21).

Findings show that when arterial occlusion time is increased beyond fifteen seconds, two factors may then account for the decrease in total resistance: active pre-venous, and passive venous segment dilatation. The active component of dilatation was abolished under conditions of hypothermia blood temperature 10-14°C). The active component of dilatation occurring in the pre-venous segment, may be produced in part by the release of histamine which dilates renal vessels (26), or some undefined vasodilator metabolite. Previous reports have discussed the possible role of histamine or other dilator agents in the reactive hyperemia response in vascular beds other than the kidney (8-10, 12-15, 17).

Pre-venous vascular responsiveness to the pressor agents epinephrine and angiotensin was found to be significantly depressed following arterial occlusion. This unexpected finding would explain a greater tendency for vasodilatation to occur in the post-occlusion period. Vascular responsiveness to histamine has been reported to be unchanged following arterial occlusion (14).

The above forces appear to account for the presence of post-occlusion hyperemia in the kidney. Of interest was the observation of a post-occlusion increase in resistance under certain experimental conditions. This post-occlusion response, termed "reactive ischemia" was particularly evident when the occlusion time was extended or when the pre- and post-occlusion arterial pressure was in the hypotensive range (40-60 mm. Hg). It appears that the forces for vasodilatation are ultimately overcome under certain conditions so that an ischemic response is observed in the post-occluded period. The forces for vasoconstriction appear to be limited in large part apparently released from kidney tissue during the occlusion period. The fairly effective actions of adrenergic blocking compounds confirmed an active role of adrenergic-like agents in the ischemic phenomenon. Angiotensin may have contributed to the constriction demonstrated as intra-arterial injections produced resistance changes similar to that of the occlusion itself, and since the constriction was sometimes a delayed response. Post-occlusion ischemia was often observed at post-occlusion arterial pressures below the autoregulatory range. This may be accounted for on the basis that the venous segment accounts for little change in resistance at this level (24, 25) and the pre-

ence of ischemic factors may be more readily revealed at lower flow rates.

The early temporary increase in pre-venous resistance observed during the post-occlusion period appears to meet the criteria for the Bayliss myogenic response (7, 28). Although only of a fleeting nature, it adds a small fraction of resistance increase to the post-occlusion response. Neither this temporary increase in resistance nor the tendency for reactive ischemia in the low arterial pressure range appears to be due to the effects of vessels which have critically closed (29) during the occlusion period. A critical closing pressure has not been found in the kidney preparation utilized in the present study (30).

The complete nature of the post-occlusion ischemic response is not clear. It is not dependent on renal innervation and therefore appears to have no counterpart in other vascular beds (11). The tendency for a post-occlusion ischemic response to occur at low arterial pressures, coupled with the effect of increased time of occlusion on intensifying the severity of ischemia may account for the particular susceptibility of the kidney to injury during prolonged systemic hypotension or shock (31).

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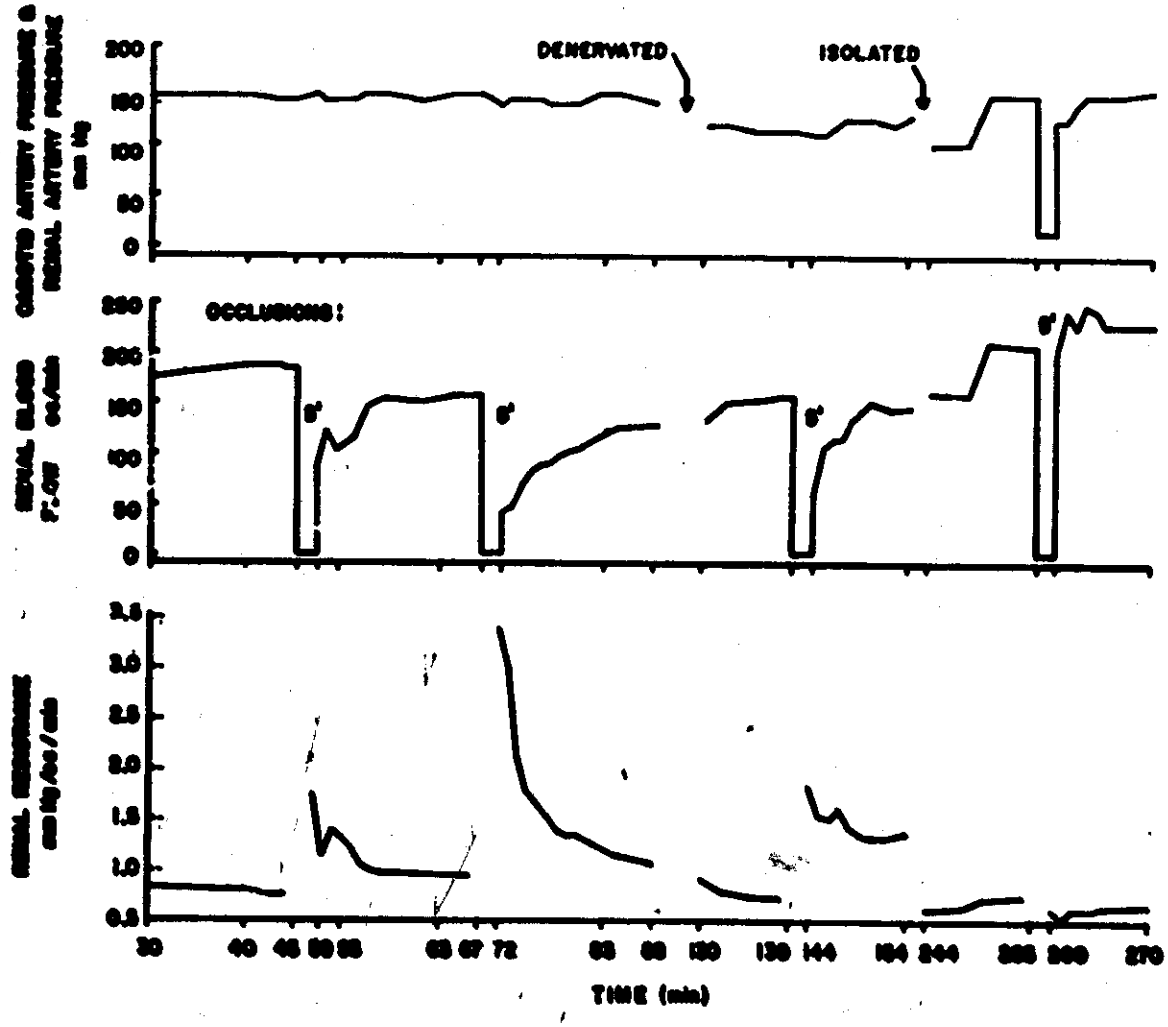

Figure 1. The effect of temporary renal artery occlusion on renal hemodynamics in the intact and isolated perfused kidney. (one experiment)

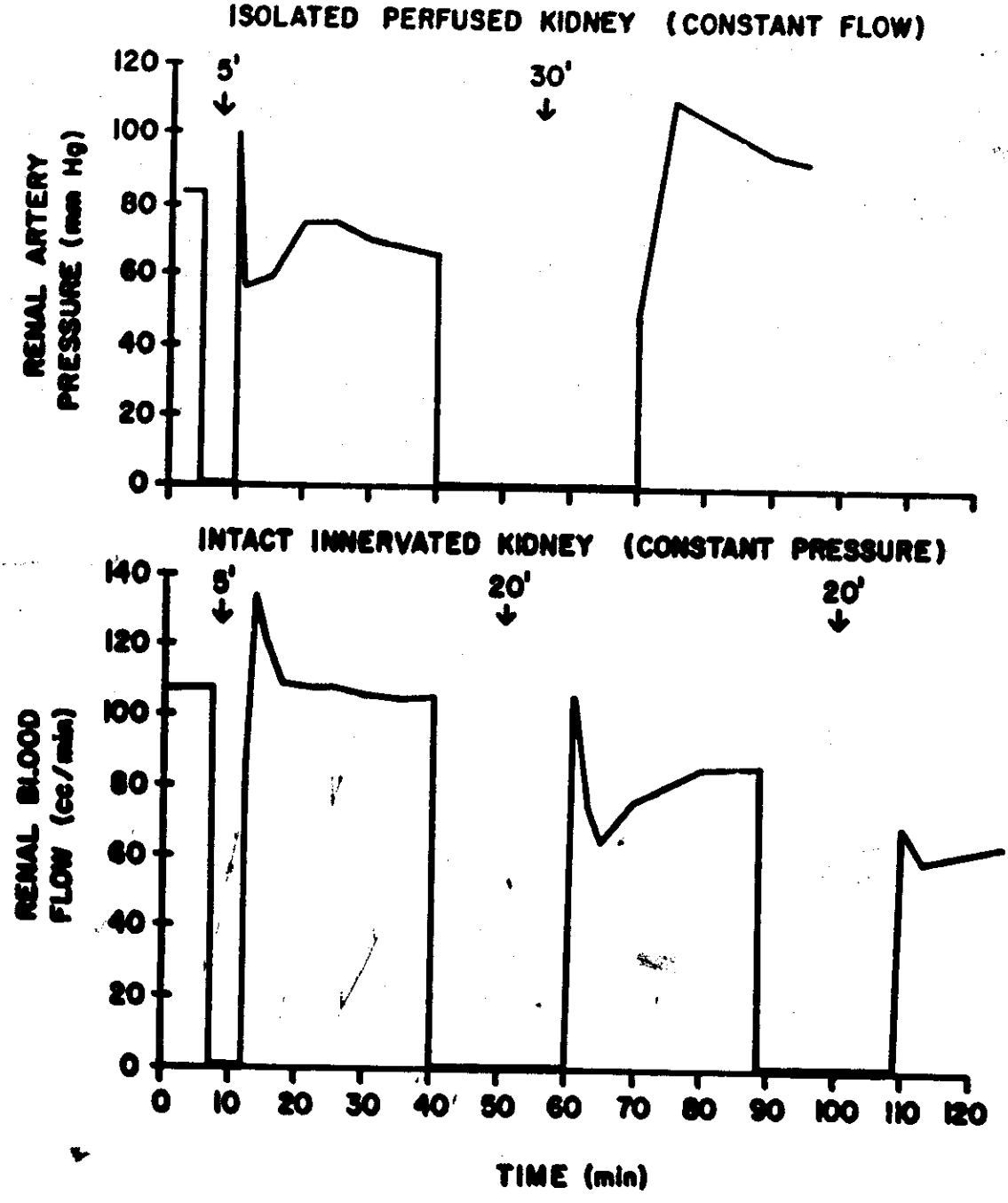

Figure 2A. The influence of time of arterial occlusion on the post-occlusion hemodynamic responses of intact and isolated perfused kidneys. (two experiments)

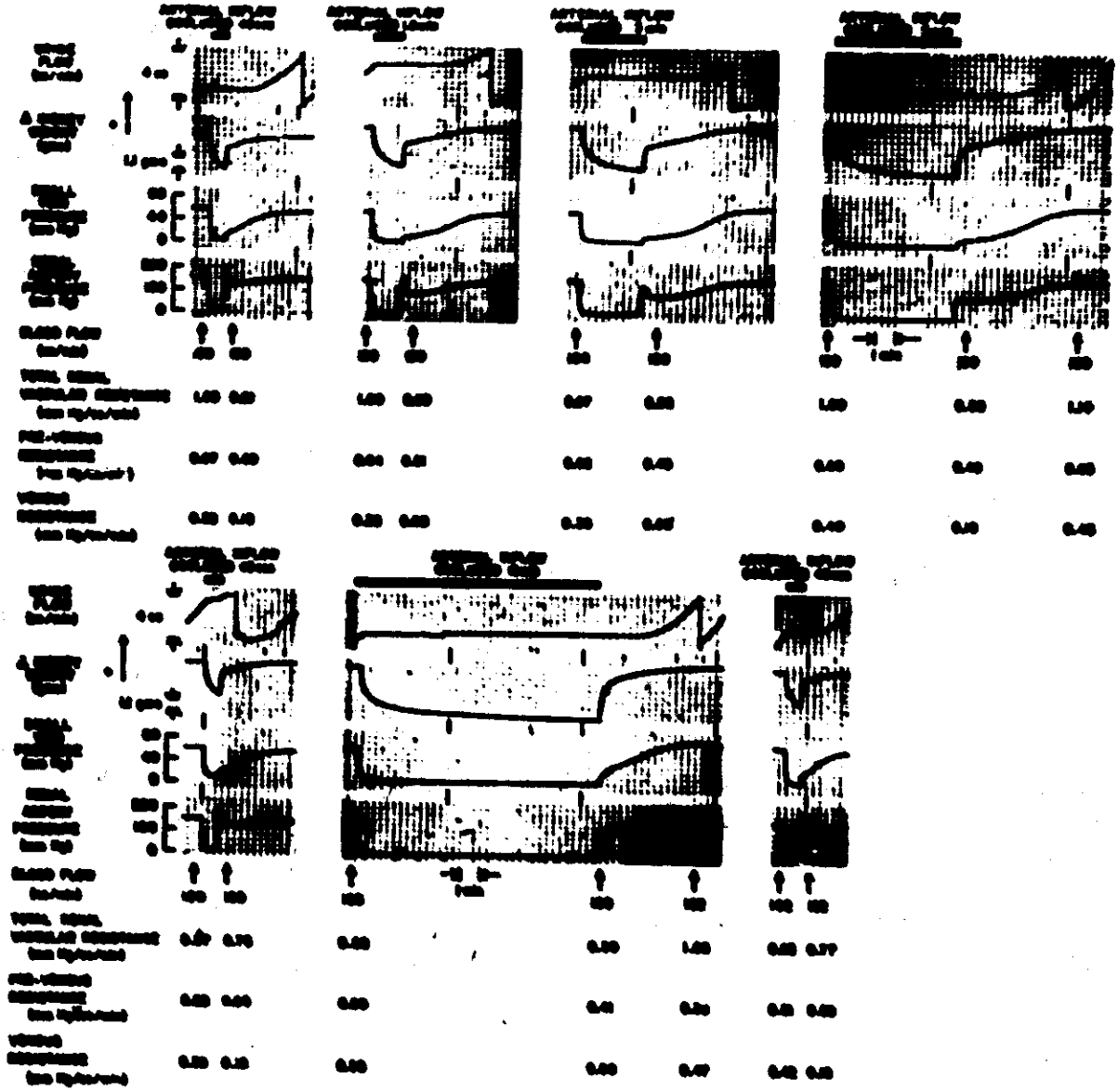

Figure 2B. The influence of time of arterial occlusion on renal hemodynamic responses (one heart-lung perfused kidney experiment)

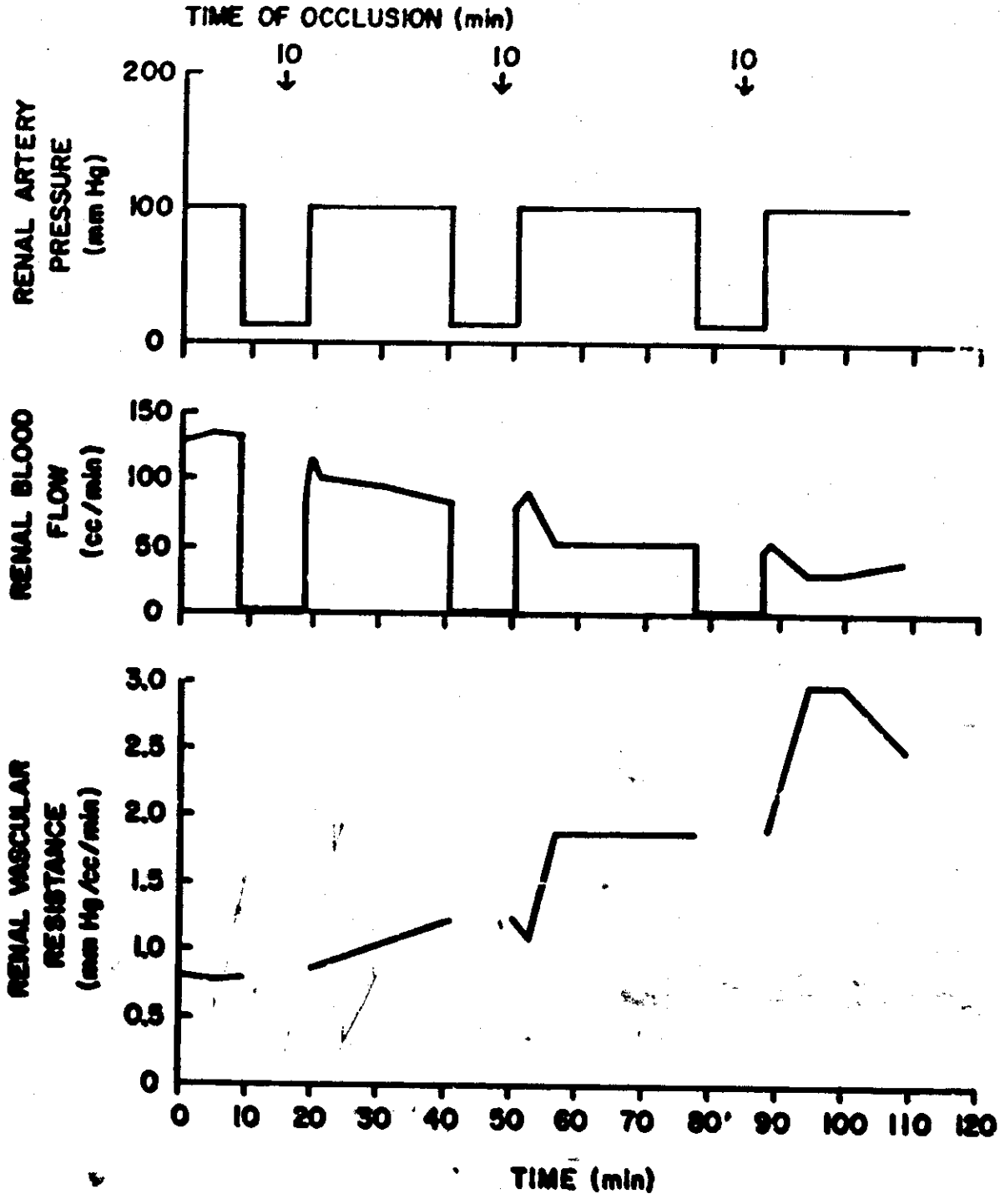

Figure 3. The effects of repeated occlusions of equal time on renal hemodynamic responses. (one dog-pump perfused kidney experiment)

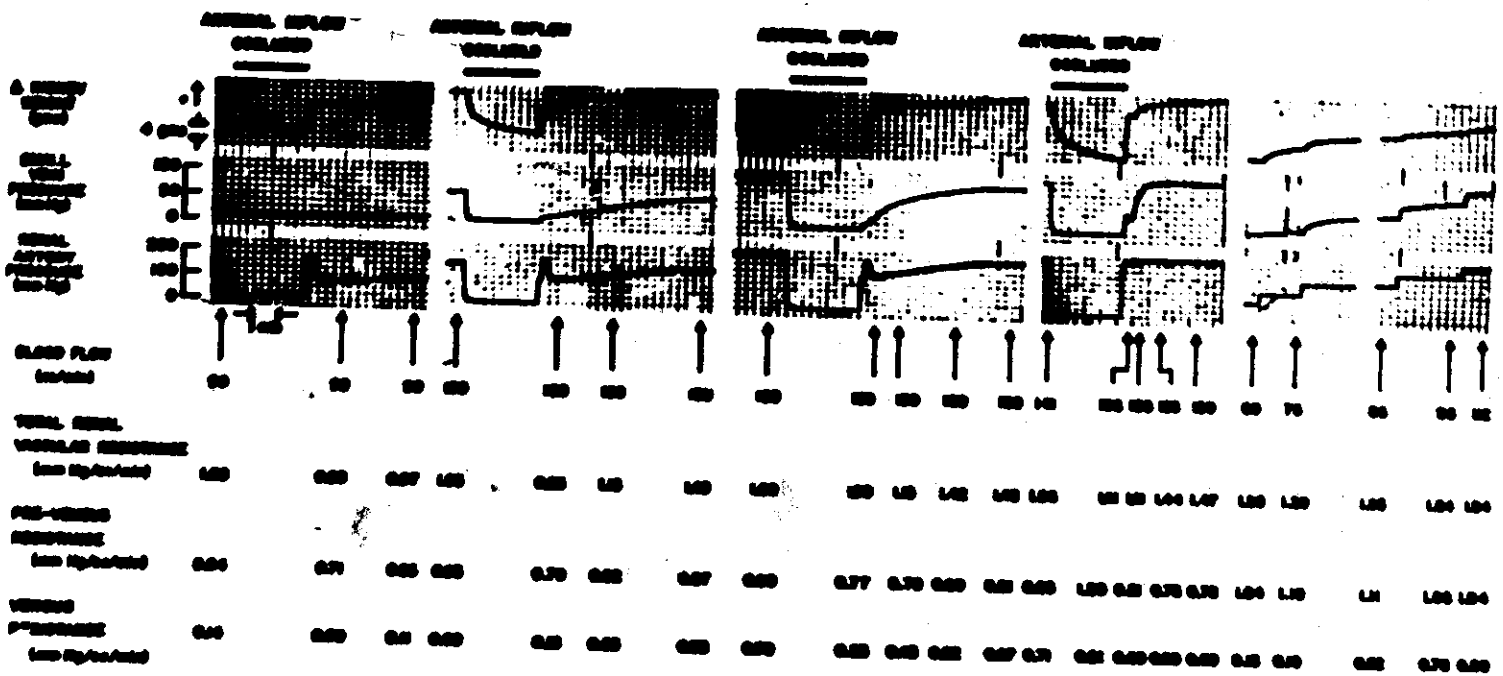

FIGURE 4. The influence of renal artery pressure on the hemodynamic responses to arterial occlusion. (one dog-pump perfused kidney experiment)

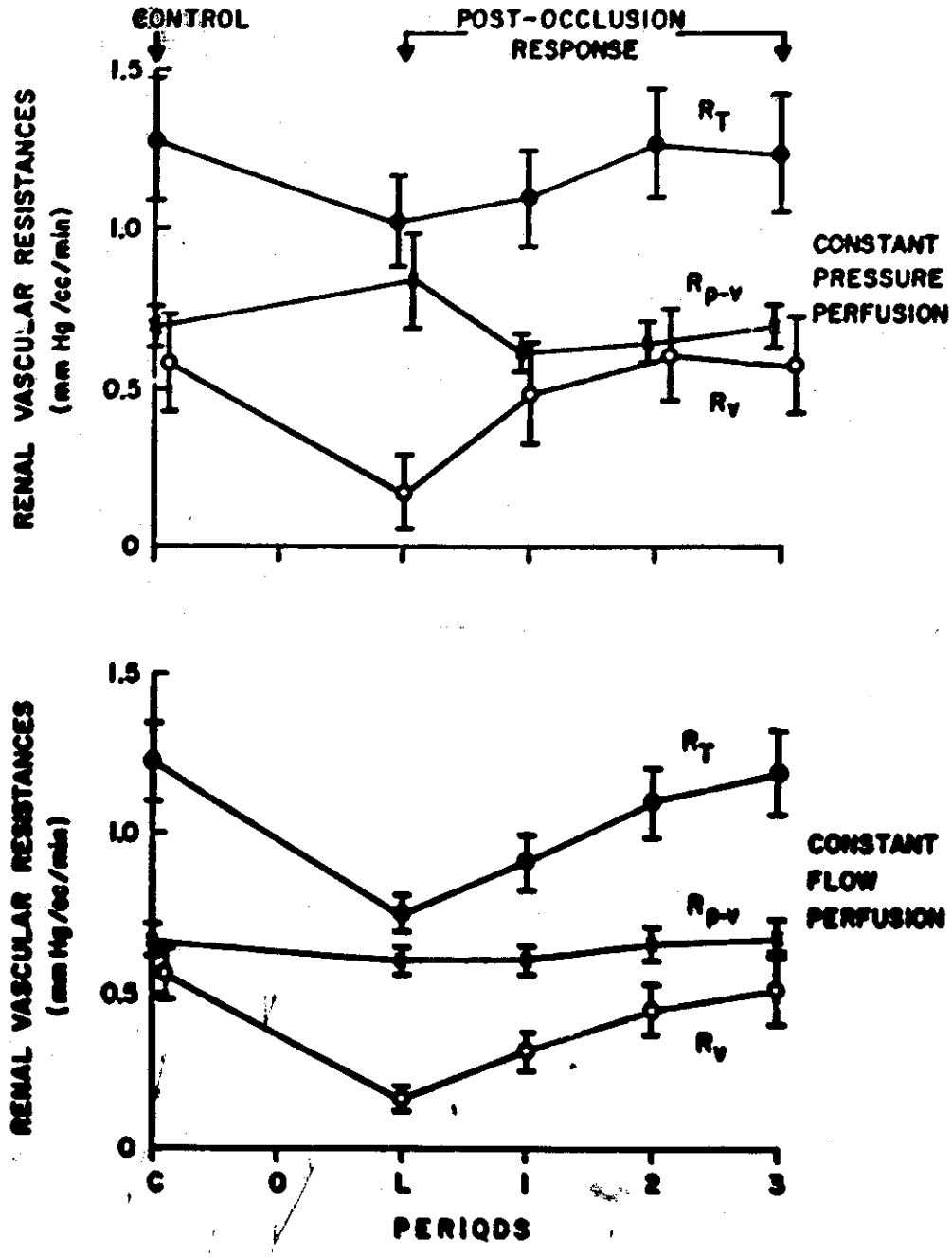

Figure 5A. Changes in renal segmental resistance following a three minute period of arterial occlusion. (mean values ± S.E.) (isolated perfused kidneys)

Upper frame: Five experiments at constant arterial pressure perfusion.
Lower frame: Seven experiments at constant arterial inflow perfusion.
R_T = Total resistance
R_{p-v} = Pre-venous segment resistance
R_v = Venous segment resistance
C = Pre-occlusive values
L = Maximum decrease in total resistance
1, 2, 3 = Recovery points

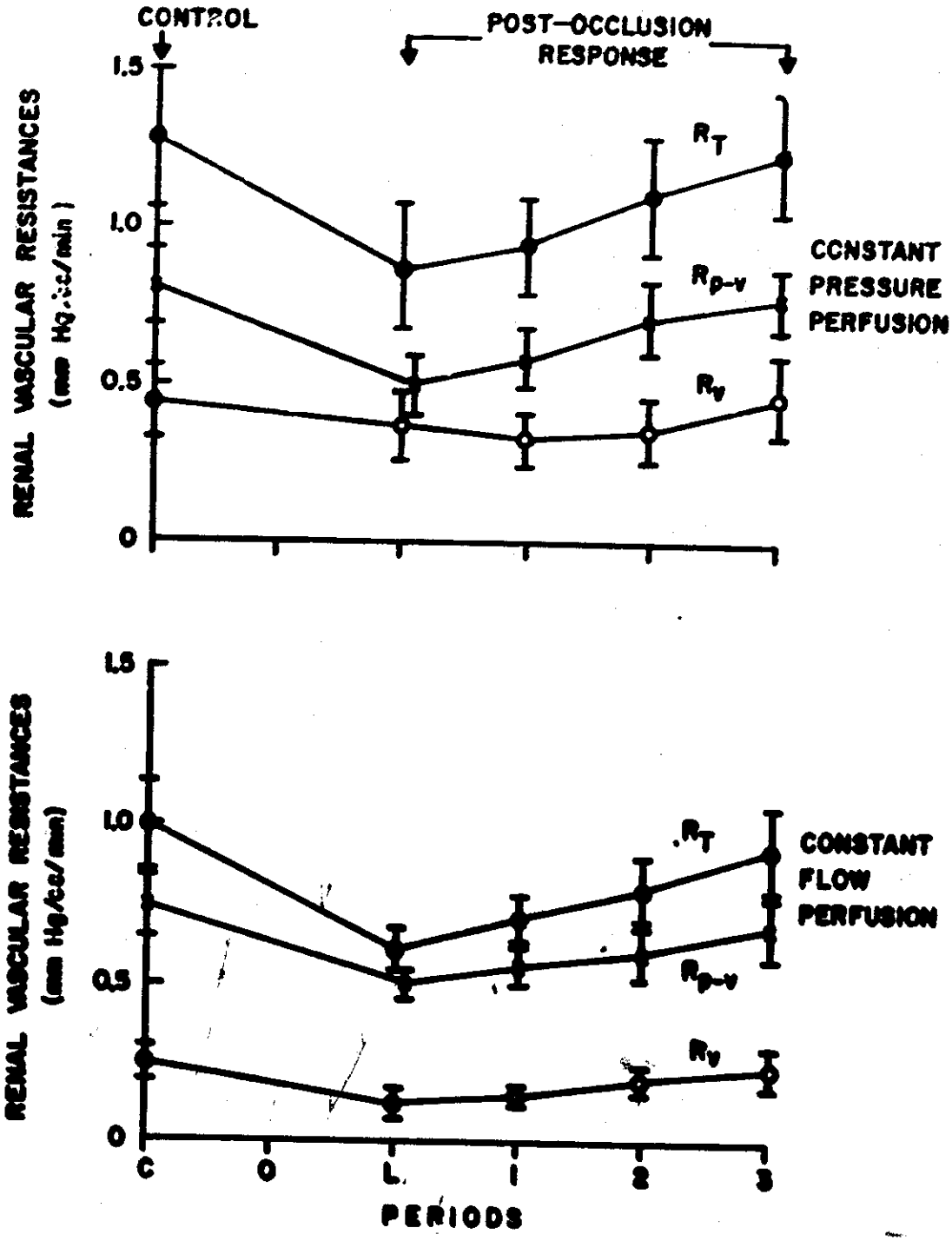

FIGURE 5-B. Changes in renal segmental resistances following a three minute period of arterial occlusion. (mean values ± S.E.) (isolated perfused kidneys)
Upper frame: Six experiments at constant arterial pressure perfusion.
Lower frame: Seven experiments at constant arterial inflow perfusion.
For symbols, see Figure 5A.

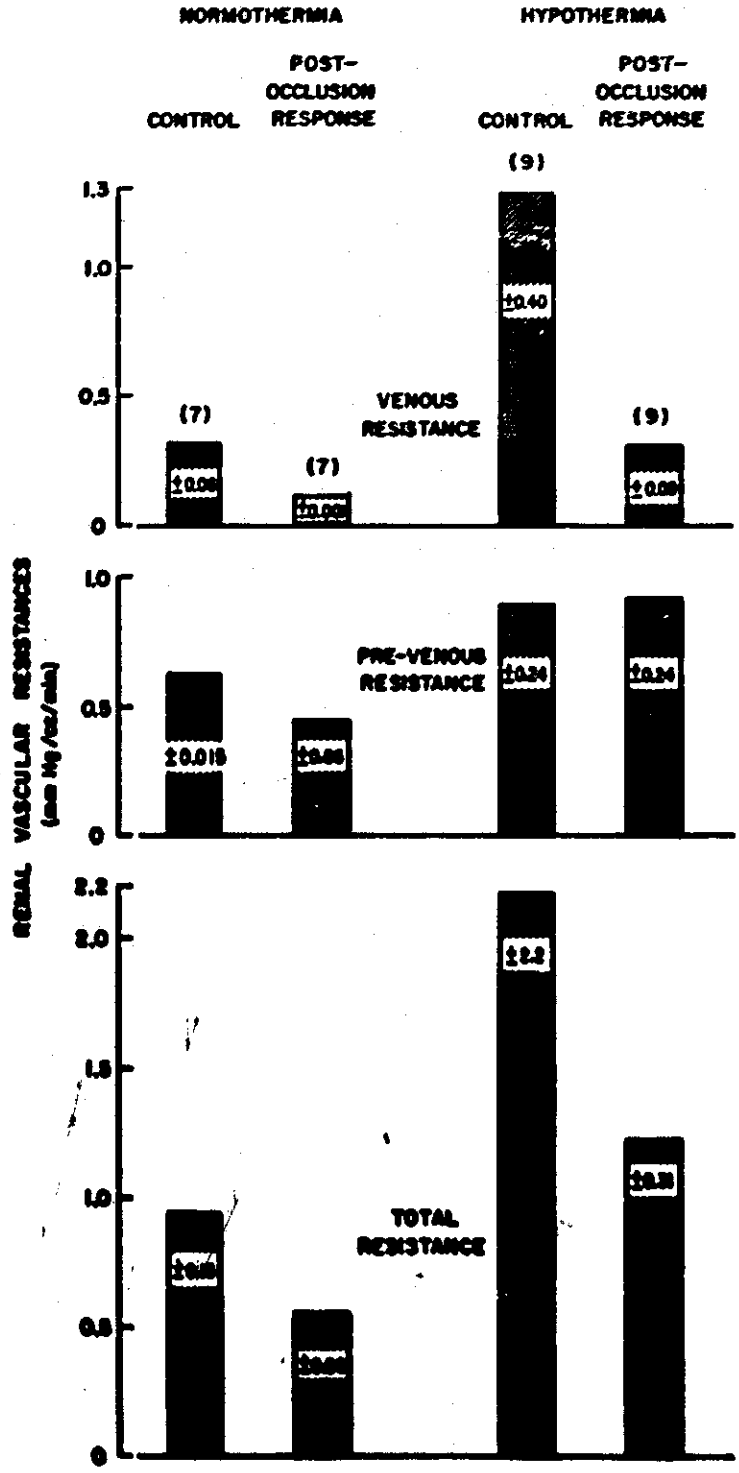

Figure 6A. The effect of lowered blood temperature on segmental resistances following arterial occlusion. (mean values ± S.E.) (five heart-lung perfused kidneys) (Numbers at top of bars are number of experiments)

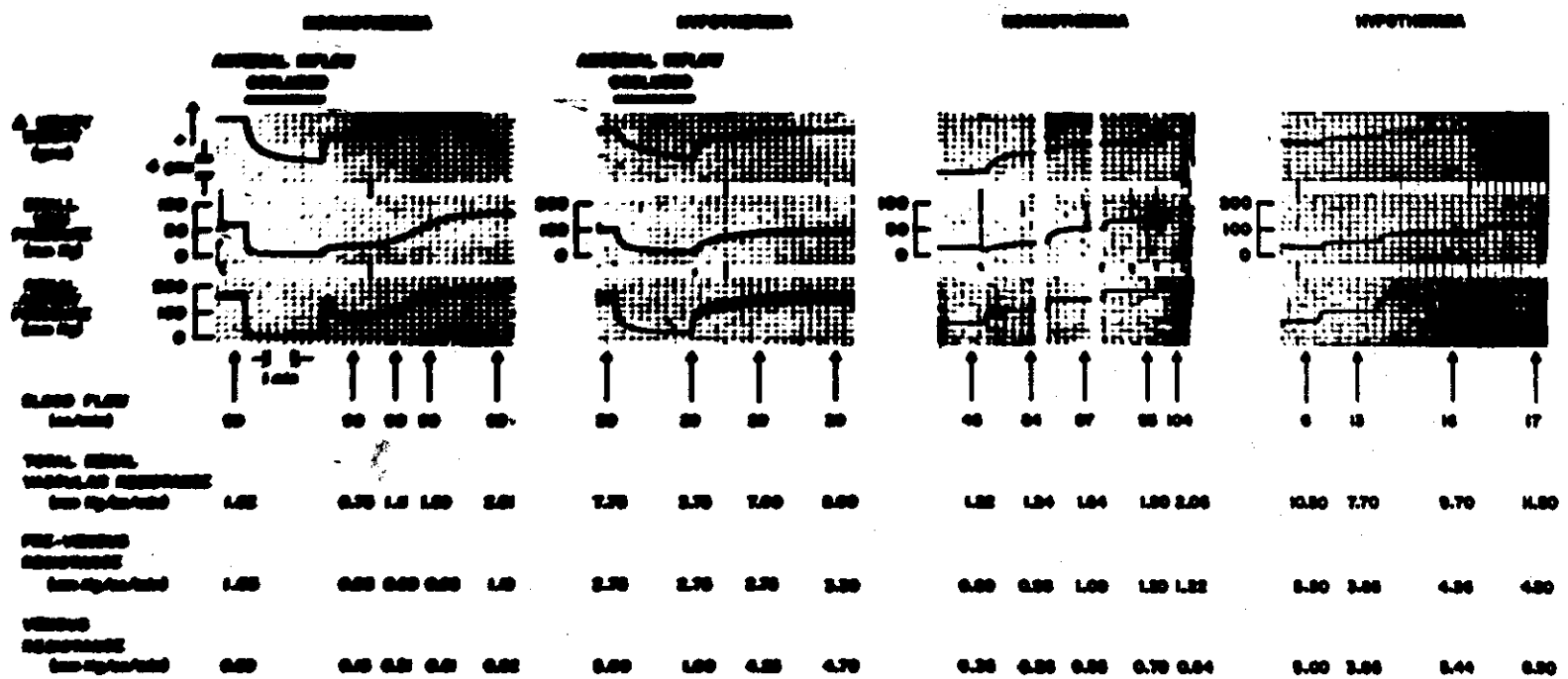

FIGURE 68. The effect of lowered blood temperature on hemodynamic responses following arterial occlusion. (one heart-lung perfused kidney experiment)

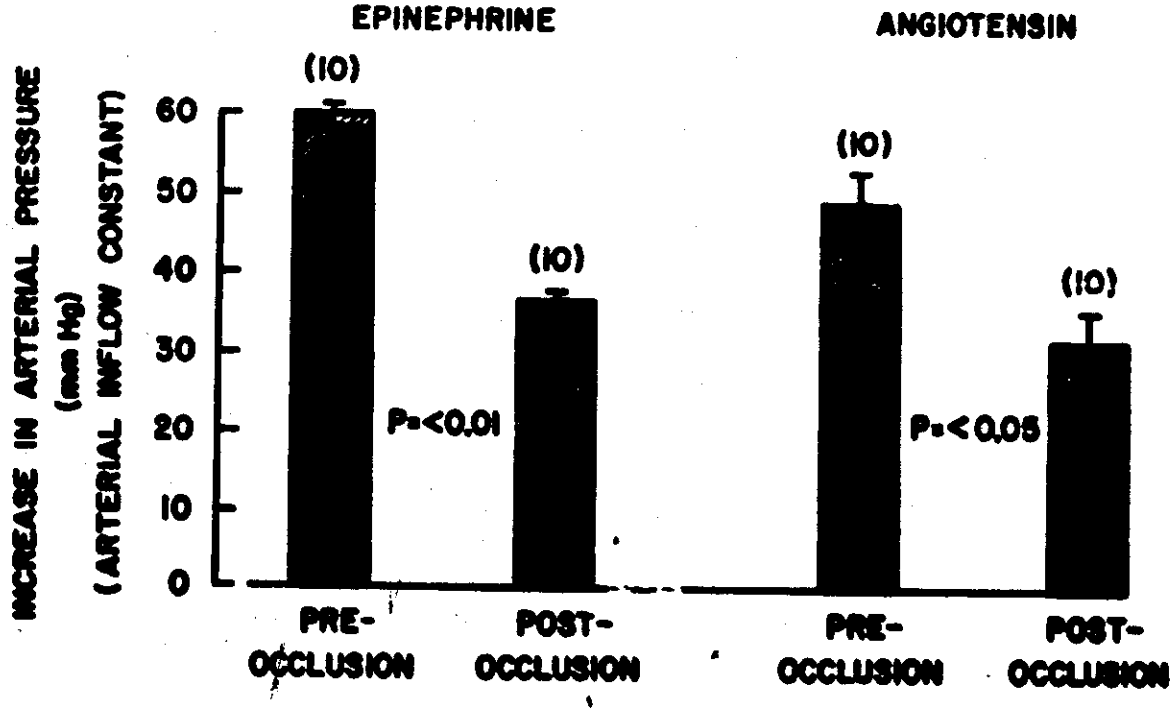

FIGURE 7. The effect of arterial occlusion on renal vascular responses to epinephrine and angiotensin. (mean values ± S.E.) (ten experiments on six dog-pump perfused kidneys)

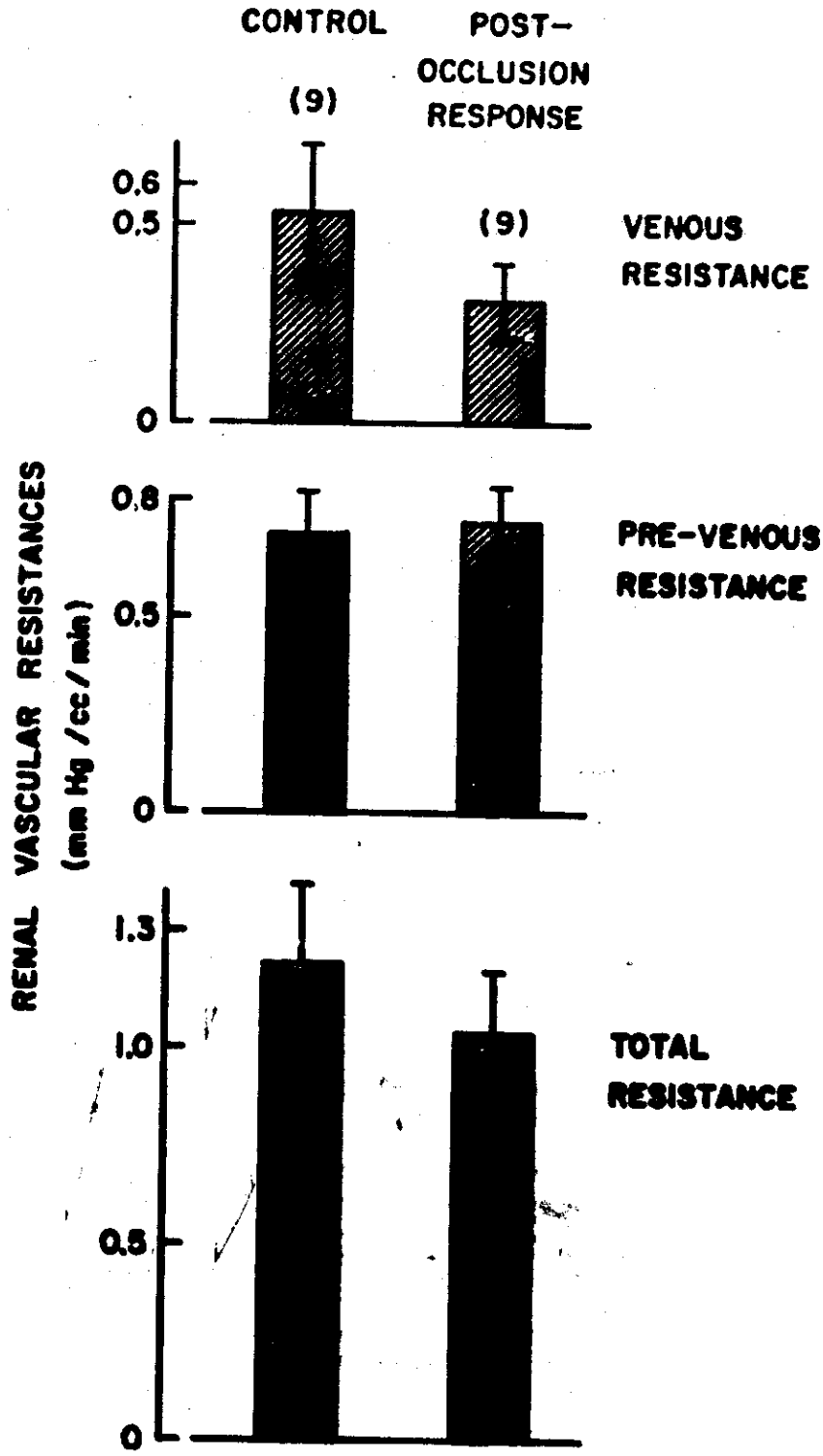

Figure 8. The effect of fifteen second arterial occlusion periods on renal segmental resistances. (mean values ± S.E.) (nine experiments on seven heart-lung perfused kidneys)

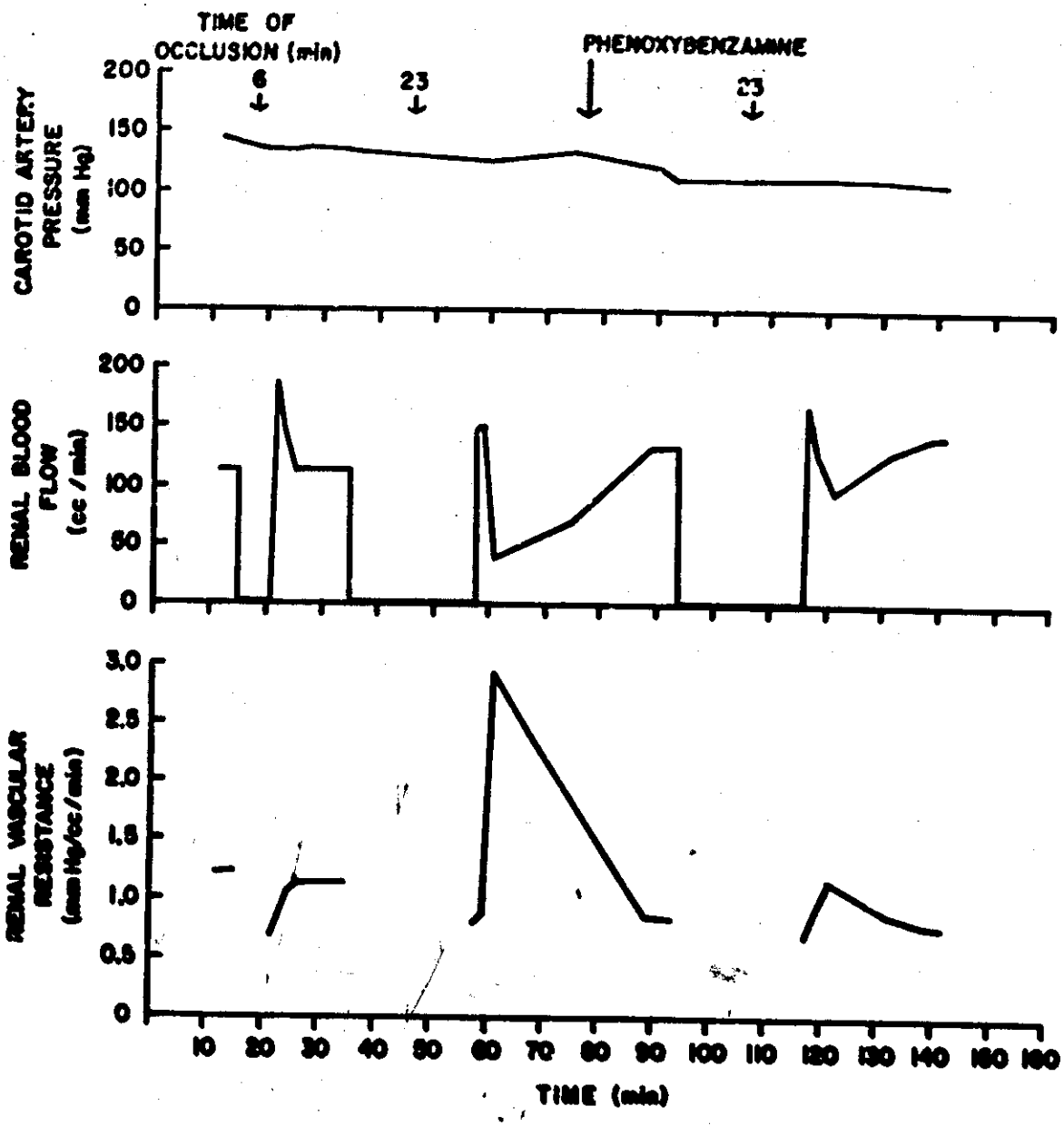

FIGURE 9. The effect of phenoxybenzamine on the renal vascular response to arterial occlusion (one typical kidney experiment)

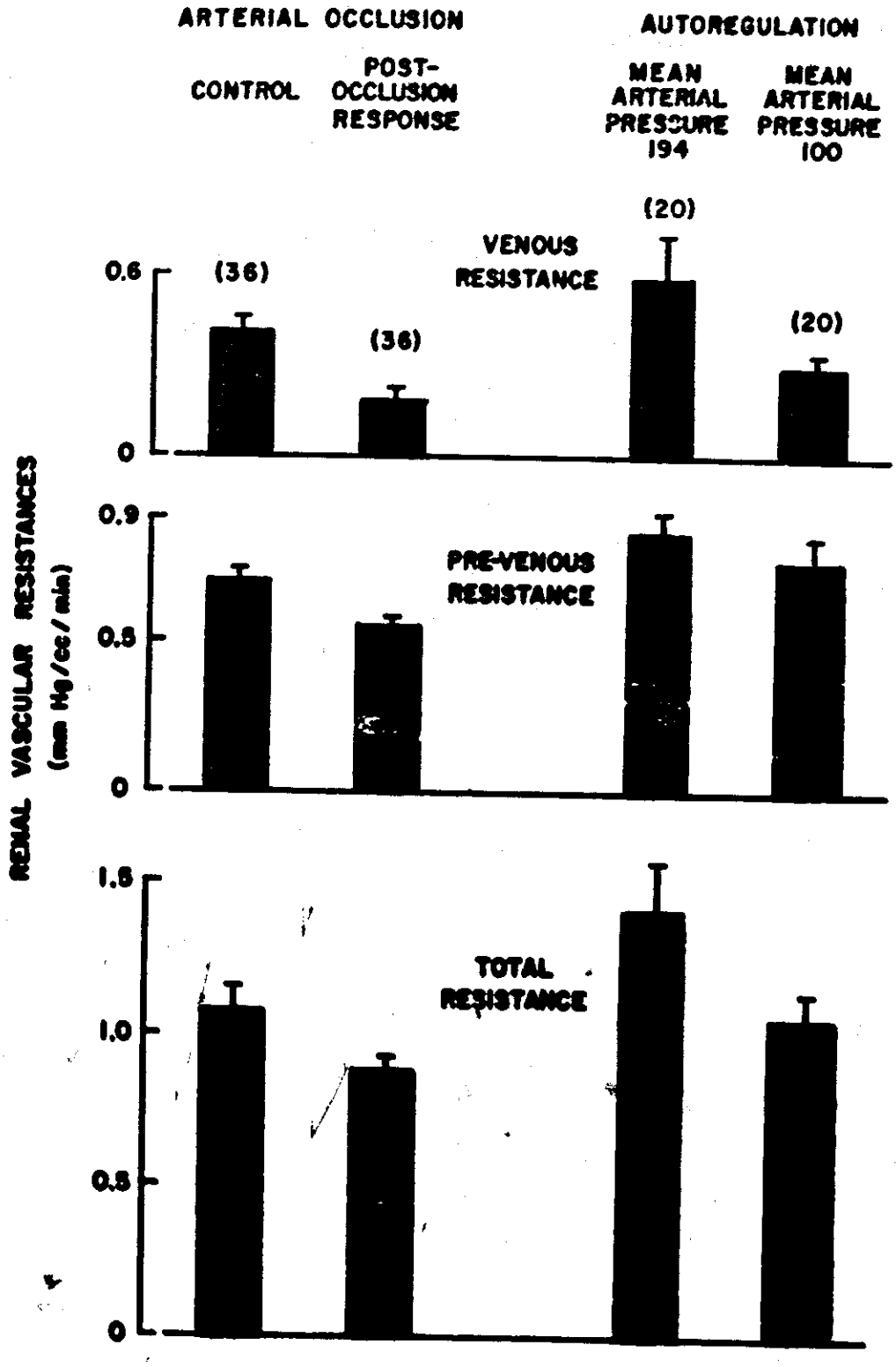

FIGURE 10. A comparison of renal segmental resistance changes following a decrease in arterial pressure and following arterial occlusion. (mean values ± S.E.) (fifteen heart-lung perfused kidneys) (numbers at top of bars refer to numbers of experiments)

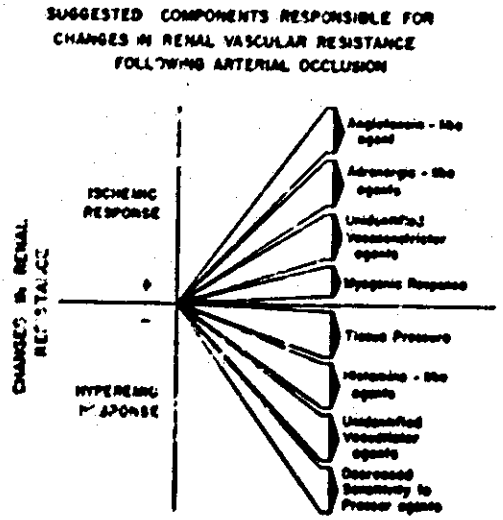

FIGURE 11. Schema.

TABLE I

EFFECT OF TIME OF OCCLUSION ON THE POST-OCCLUSION RESPONSE OF THE KIDNEY

Intact kidneys (Expt. No.)	Time of occlusion 15"-60"	90"-5'	6'-20'	21'-30
1*		RH†		RI†
2**		RH	RI	
3**	RI	RI	RI+	
4**		RH	RI	
5*		RI	RI+	
6**		RH	RH	
7*	RI	RI		
8**		RH	RH	
Isolated kidneys (perfused)				
1		RH	RI	
2	RH	RH	RI	
3		RH	RI	
4	RH		RI	
5	RH	RH	RH	
6	RH	RH	RI	
7	RH		RH−	
8	RH	RH	RH−	
9	RH	RI	RI	

†RH = decrease in renal resistance following occlusion
†RI = increase in renal resistance following occlusion
(+ and − refer to degree of response compared to previous response)
* Denervated
** Innervated

TABLE II

EFFECT OF POST-OCCLUSION RENAL ARTERY PRESSURE ON THE POST-OCCLUSION VASCULAR RESPONSE

Renal Artery Pressure Ranges: (mmHg)			45-55			100-125			140-183	
Experiment #	Time of Occlusion (min)	Renal Artery Pressure (mm Hg)	Renal Blood Flow (cc/min)	Maximum % Change in Renal Blood Flow	Renal Artery Pressure (mm Hg)	Renal Blood Flow (cc/min)	Maximum % Change in Renal Blood Flow	Renal Artery Pressure (mm Hg)	Renal Blood Flow (cc/min)	Maximum % Change in Renal Blood Flow
1	5	50	102	−22%	100	264	+65-7%	150	291	+22%
2	3	45	111	−32%	100	171	+ 5%	140	200	+ 9%
3	3	50	7	−57%	100	80	+11%	150	108	+24%
4	3	50	72	−58%	102	140	−21%	160	138	+ 8%
5	3	50	120	−25%	100	224	−11%	150	280	+ 4%
6	3	50	98	+ 6%	100	186	+15%	175	216	+ 8%
7	3	55	111	+22%	125	120	+37%	180	213	+31%
8	3	58	36	+14%	100	62	+26%	183	105	+26%
9	3	50	54	+ 4%	100	74	+14%	150	87	+25%
MEAN (±S.E.)	3.5 ± 0.3	51 ± 1.2	88 ± 16	−16.6% ± 9.9	103 ± 2.7	151 ± 23	+8.9% ± 6.9	160 ± 5	152 ± 25	+17.4% ± 3.3
Mean Pre-Occlusion Resistance (mmHg/cc/min)			0.59			0.66			0.88	

TABLE III

EFFECT OF ADRENERGIC AND HISTAMINE BLOCKING AGENTS ON THE POST-OCCLUSION ISCHEMIC RESPONSE

Exp. #	Preparation	Occlusion Time (min)	Post Occlusion, Control	Max. % Δ in R_v	Effect of Phenoxy-benzamine*	Drug Response** E	NE	A	H	Occlusion Post Phenoxy-benzamine	Max. % Δ in R_v	Occlusion Post-Diphenhy-dramine	Max. % Δ in R_v	Drug Response A	H
1	Dog-pump-kidney	16	RH → RI	+23%	RI abolished	+	+	−	+	RI †	+19%				
2	" " "	5	RI	+32%	RI not "	+	+	−	−	RI‡	−37%	RI	+27%	−	+
3	" " "	15	RI	+25%	RI abolished	+	+	−		RI	+19%	RI	+38%	+	+
4	" " "	15	RI	+21%	RI not "	+	+	−	−	RI‡	+33%				
5	" " "	3	RI	+24%	RI abolished	+	+	+	−	RI	+13%	RI	+29%	−	+
6	" " "	10	RI	+22%	RI not "	+	+	−	+	RI‡	+27%				
7	" " "	10	RI	+23%		+				RI	+17%				
8	Intact Kidney (innervated)	6	RI	+55%						RI††	0%				
9	"	10	RI	+50%						RI††	0%				
10	Intact Kidney (denervated)	23	RI	+59%						RI††	0%				
Means	(± S.E.)	11.3		+30% ± 5							+9% ± 6				

* Phenoxybenzamine injected during ischemic response
** Successful block = +
Failure to block = −
E = epinephrine
NE = nor-epinephrine
A = angiotensin
H = histamine

† RI abolished with phentolamine
‡ RI not affected with phentolamine
†† RI only temporary (i.e. returned to control within approx. 10 mn.)

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the arterial pressure. The combined effects of pre-venous dilatation and diminished tissue pressure resulted in a decreased resistance following shorter periods of occlusion. Pre-venous dilatation was accounted for by depressed vascular sensitivity to pressor agents and the presence of vasodilator substances. Changes in venous segment resistance were found to be of primary importance in both the autoregulatory phenomenon and the post-occlusion hyperemic response to short (fifteen second) occlusion periods.

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2. Renal Ischemia
3. Renal Hypoxia
4. Renal Arterial Occlusion
5. The Kidney and Vascular Resistances
6. The Kidney as a Secretor of Constrictors and Dilators
7. Renal Stress

The hemodynamic response of the kidney to acute arterial occlusion is poorly understood. The purpose of the present study was to determine intrarenal hemodynamic changes in intact and isolated kidneys following arterial occlusion. The relative roles of metabolic, myogenic and tissue pressure influences on the post-occlusion response were evaluated. The response of the kidney to occlusion was found to be complex depending on the interaction of a variety of physical and humoral forces. Increases in renal resistance appeared to be due in part to adrenergic agents and were enhanced by extending time of occlusion and lowering

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