

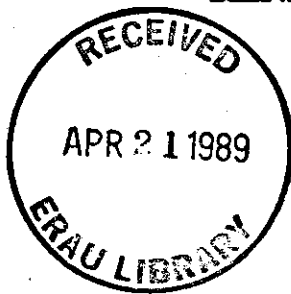
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**EFFECT OF INCREASED
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RENAL HEMODYNAMICS**



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OKLAHOMA CITY, OKLAHOMA

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CHARLES M. BRAKE

P. F. IAMPIETRO

THOMAS E. EMERSON, JR.

with the assistance of

Fred D. Masucci

Rosalie A. LaVon

Environmental Physiology Branch

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ABSTRACT

Conflicting evidence exists in regard to the effects of increased venous pressure on renal hemodynamics. Experiments to clarify its role were carried out on twenty-eight intact innervated or isolated perfused dog kidneys. Findings indicate the absence of a "venous-arteriolar" reflex. Decreases in total resistance occur as venous pressure is increased through a wide range in both innervated and isolated perfused kidneys. Intrarenal venous and tissue pressures and blood flow are unaffected by large increases in venous pressure, (21-75 mm. Hg), although venous segment resistance declines markedly. Decreases in blood flow are seen when renal vein pressure approaches or exceeds intrarenal venous and tissue pressures. Results confirm previous investigations regarding the importance of tissue pressure and intrarenal venous pressure in renal hemodynamics, which appear to "buffer" the kidney against effects of elevated venous pressure through a variable but unusually large venous pressure range. The phenomenon of autoregulation may be extended to include a tendency for renal blood flow constancy in the face of wide swings in both renal artery and venous pressures.

INTRODUCTION

The effect of increased renal venous pressure on renal hemodynamics is poorly understood and there is considerable conflict in the results obtained by various investigators (1-6). Attempts have been made to assay the role of venous pressure in certain clinical conditions, but its effect on renal pressure-flow relationships is debatable (7). Haddy and others (3, 6) reported an increase in renal resistance in the innervated kidney and a decrease in the denervated kidney as a function of renal vein pressure elevation. On the other hand, Ochwaldt (4) and Waugh and Hamilton (3) observed an increase in renal resistance in the isolated perfused kidney as a result of elevation of renal vein pressure. Ochwaldt considered his findings to bear on the mechanism of renal autoregulation as was also suggested by Semple and de Wardener (8). Waugh and Hamilton

pointed out that elevated renal vein pressure increased total renal vascular resistance by increasing interstitial pressure (5).

These previous investigations did not take into consideration the recent observations (9, 10), that through the renal artery pressure range from 70 to 200 mm. Hg, there are large differences between orifice renal venous pressure and deep intrarenal venous pressure. The original aim of the present investigation was to elucidate the mechanism of increased renal resistance following elevation of renal vein pressure, with particular reference to the roles of deep intrarenal venous and tissue pressures. Results, however, do not confirm the studies of previous investigators (3-6), but show a decrease in total renal vascular resistance as a function of increased venous pressure in both intact innervated and isolated perfused kidneys. The implication of these findings is discussed.

METHODS

This investigation was divided between studies on intact innervated and isolated perfused dog kidneys. Sixteen experiments were carried out on the isolated heart-lung perfused kidney. The experimental preparation has been previously described (11-13).

The heart-lung kidney preparation was utilized in all isolated perfused kidney experiments. Adult dogs were administered sodium pentobarbital, the left kidney was removed without interruption of renal blood flow and perfused with heparinized homologous blood at a controlled renal artery pressure. The orifice renal vein was cannulated with a 3-5 cm. length of polyethylene tubing fitted with a rubber sleeve for needle insertion. An adjustable screw clamp was placed distal to the rubber section and was used to alter renal vein pressure. Intrarenal venous pressures were obtained by advancing a small polyethylene catheter (O.D., 0.7 mm.) through the renal vein deep into the kidney substance (9, 10). Tissue pressures were obtained by inserting a No. 23 needle into the kidney parenchyma and connecting the needle to a Statham pressure transducer by means of a saline filled catheter (13). Renal blood flow and urine flow were measured with a graduated cylinder and stopwatch.

The magnitudes and directional changes of tissue pressure and deep intra-renal venous pressure were similar, as has been reported previously (9). All pressures were obtained from catheters attached to pressure transducers and registered on a Sanborn direct writing recorder. Orifice renal vein pressure was increased in stepwise fashion through a wide range (0-100 mm. Hg). Venous pressure was maintained at each pressure level from 4 to 6 minutes until pressures and flows became stabilized. Changes in the following parameters were observed as a function of elevated renal venous pressure (RVP): intrarenal venous pressure (IRVP), tissue pressure (TP), renal segmental vascular resistances: $R_{1,1}$ (prevenous or intrarenal resistance), R_s (venous segment resistance), R_t (total renal resistance), renal blood flow and

urine flow. Control blood flows in isolated kidneys averaged 2.8 cc./min./gm. (range, 1.5-4.9).

Experiments were also carried out on seven intact innervated kidneys and five isolated kidneys. In the latter instance, results from constant flow and constant pressure perfusions were compared. Procedures used in the intact innervated kidney experiments have been previously described (11). Renal vein blood flow was measured with cylinder and stopwatch. The renal pedicle was untouched and renal vein outflow was diverted from its usual path into an extracorporeal circuit and returned to the jugular vein. Since all contaminating veins were ligated, venous outflow between pedicle and site of cannulation (inferior vena cava) was derived only from the kidney. Renal venous pressure was increased by a screw clamp placed on the venous outflow tubing and pressures were measured at the site of the orifice renal vein. Venous pressures were maintained at each level until successive blood flows were in close agreement (3-8 min.). Mean aortic pressures averaged 126 mm Hg. and mean control renal blood flows were 3.2 cc./min./gm.

RESULTS

Figures 1 and 2 illustrate findings from two isolated perfused kidney experiments which are representative of results obtained at different renal artery, intrarenal venous and tissue pressures. Renal vein pressure is increased in stepwise fashion in each experiment. In Figure 1, renal artery pressure was maintained at 160 mm. Hg and renal vein pressure was increased from 0 to 97 mm. Hg. Renal blood flow is seen to remain relatively constant until renal vein pressure (RVP) exceeds 75 mm. Hg, a value approximately equal to control (zero time) intrarenal venous pressure (IRVP) and tissue pressure (TP).

Above this pressure, renal blood flow shows a marked fall from 124 to 99 cc./min., and RVP, IRVP and TP then rise together in an approximate 1:1 ratio. Urine flow, on the other hand, is observed to fall at a venous pressure of 43 mm. Hg. Total renal resistance (R_t) and venous segment resistance (R_s) markedly

fall as renal vein pressure is increased, while pre-venous resistance ($R_{v..}$) remains relatively constant. It is clearly seen that the cause of the decrease in R_r is the drop in R_s segment resistance.

Figure 2 represents an experiment on another isolated perfused kidney when renal artery pressure is maintained at a lower value (108-110 mm. Hg) than in Figure 1, in which control IRVP and TP values are also less than those in Figure 1. Results are consistent with those in Figure 1, except that renal blood flow and urine flow decrease at lower renal vein pressure values. When RVP is increased, renal blood flow does not show a significant drop until RVP exceeds 25-35 mm. Hg, which approximates the control (zero time) IRVP and TP. Above this pressure RVP, IRVP and TP rise in an approximate 1:1 fashion. Again, a progressive decrease in R_r is observed as a function of an increase in RVP, which is due to a fall in R_s segment resistance. When RVP is returned to zero mm. Hg, there is a good recovery of all parameters to control values in experiments shown in Figs. 1 and 2.

Figure 3 illustrates mean values for sixteen separate renal perfusions. Individual experiments followed courses similar to those shown in Fig. 1 and 2. The maximal increase in RVP in which there was no significant change in renal blood flow is indicated in the figure and averaged 38 mm. Hg (S. E. ± 4). Mean values of measured and calculated parameters for the sixteen experiments are also shown in the figures. Renal artery pressure was maintained constant in each experiment by means of a Starling shunt device (average arterial pressure, 131 mm. Hg, S. E. ± 5). As RVP was increased to a mean value of 38 mm. Hg, there were no significant changes in blood and urine flows, IRVP and TP. Decreases in R_r and R_s were observed, with $R_{v..}$ remaining constant.

Figure 4 shows the averaged results from sixteen kidney experiments in which the lowest RVP required to produce a significant decrease in renal blood flow, is plotted against control (zero time) IRVP and TP values. These data offer evidence that renal blood flow will remain unaltered in the face of an increased renal vein

pressure until the latter approximates or exceeds the pre-existing intrarenal pressure (IRVP and TP). Points at the lower left portion of the figure were obtained from experiments in which renal artery pressure was approximately 100 mm. Hg, while those in the upper right were obtained with renal artery pressures in the range of 190 mm. Hg. This latter relationship is more in evidence in Fig. 5, in which the renal vein pressure at which renal blood flow significantly falls, is plotted against the prevailing renal artery pressure. Figures 4 and 5 combine to show that there is a good correlation between the prevailing renal artery, intrarenal venous and tissue pressures, and the required renal vein pressure necessary to elicit a significant fall in renal blood flow.

Following the conclusion of experiments on the isolated perfused kidney, a series of studies were carried out on the intact, innervated kidney. Findings from seven innervated kidneys are shown in Fig. 6. It is seen that as renal vein pressure is increased progressively from 0 to approximately 70 mmHg, there is a decrease in total renal vascular resistance. Renal artery pressures (aortic pressures) were essentially constant during each experiment and ranged between 105 and 155 mm Hg. When elevated venous pressures were restored to control values, there was a good recovery of control resistance values.

A group of experiments were then carried out on five heart-lung perfused kidneys in order to evaluate resistance effects of constant flow and constant pressure perfusion techniques. Kidneys were alternately perfused in random order at both constant renal artery pressure and constant renal blood flow. Figure 7 contrasts the results and shows that at constant flow, an elevation in RVP produces an increase in resistance in most instances, although results were variable. In experiments in which resistance rose at constant flow, up to eight minutes was required at each venous pressure level until renal artery pressures stabilized. It was also noted that changes in tissue pressure and kidney weight were greater in the constant flow perfused kidney following alteration of renal vein pressure.

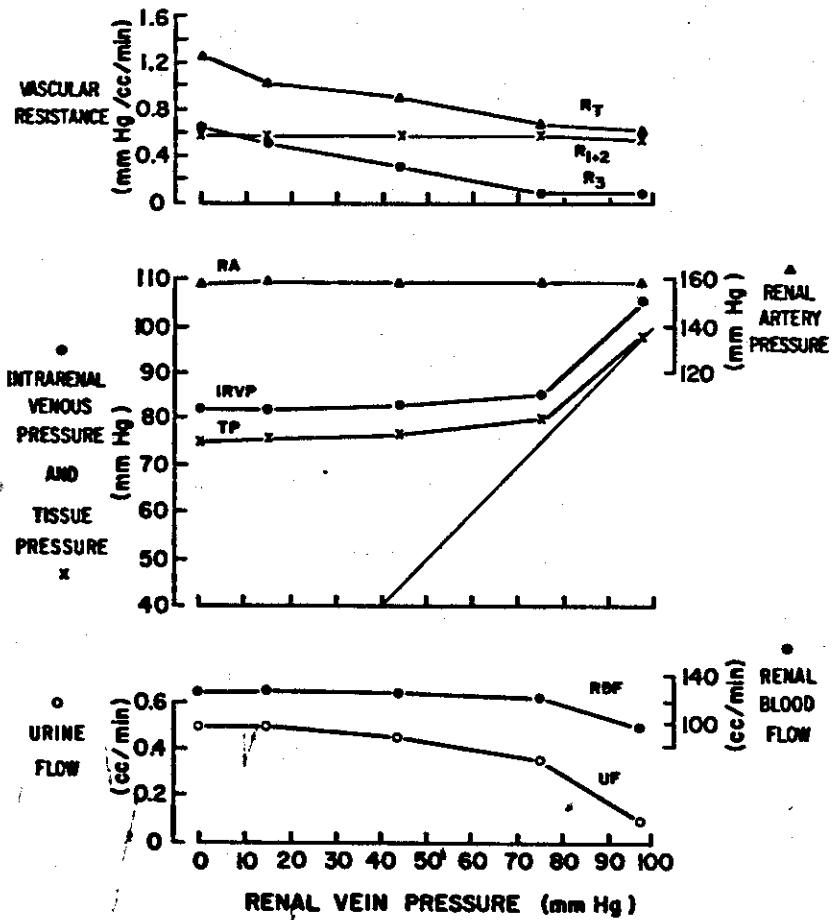


FIGURE 1. Effect of increased renal vein pressure on renal hemodynamics in the isolated perfused dog kidney.

(renal artery pressure maintained at 160 mm. Hg)

Diagonal line, middle frame, is line of unity between RVP and IRVP, TP.

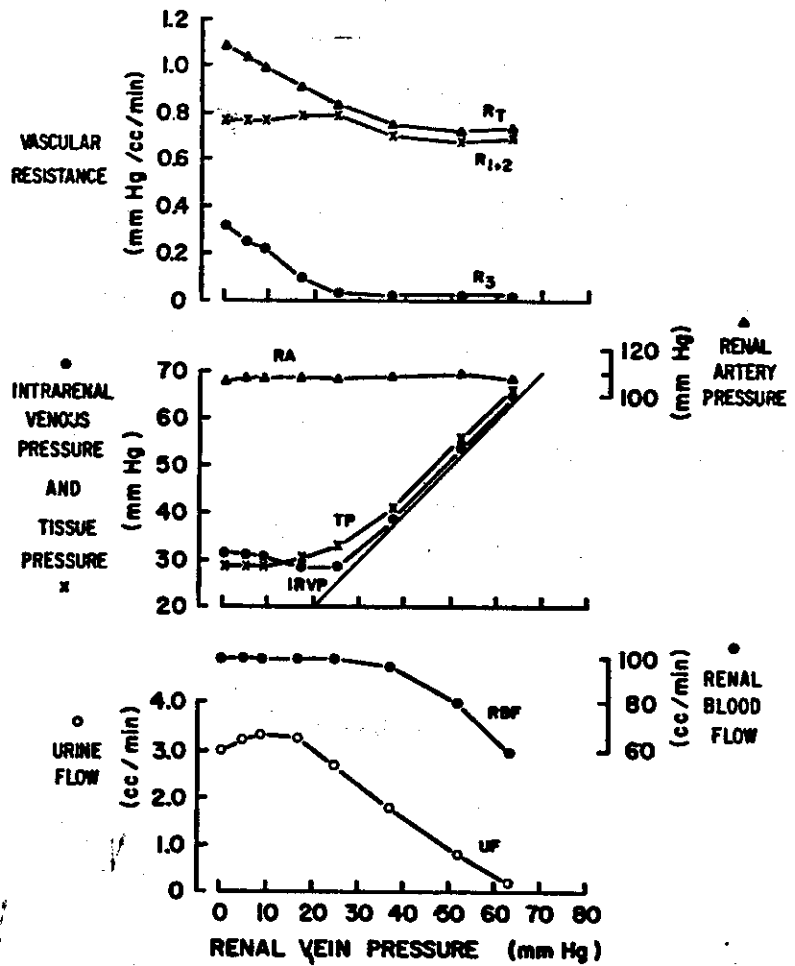


FIGURE 2. Effect of increased renal vein pressure on renal hemodynamics in the isolated perfused dog kidney.
 (renal artery pressure maintained between 108-110 mm. Hg)
 Diagonal line, middle frame, is line of unity between RVP and IRVP, TP.

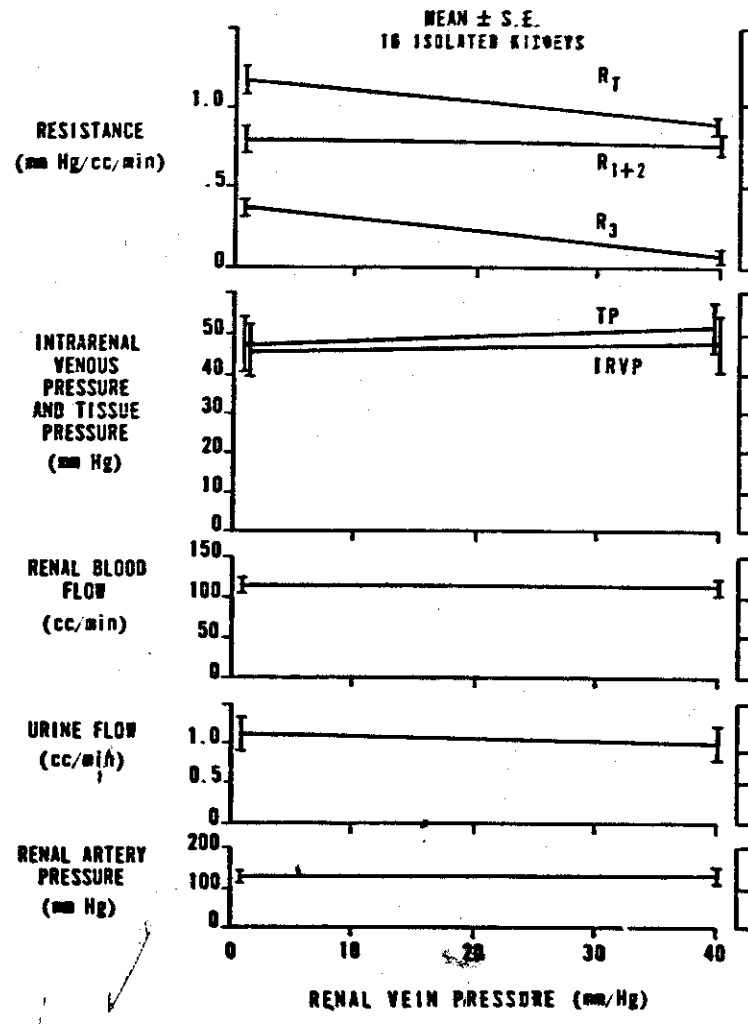


FIGURE 3. Effect of increases in renal vein pressure on the kidney. Mean values, 16 isolated perfused kidneys.
(renal artery pressure maintained constant in each experiment)

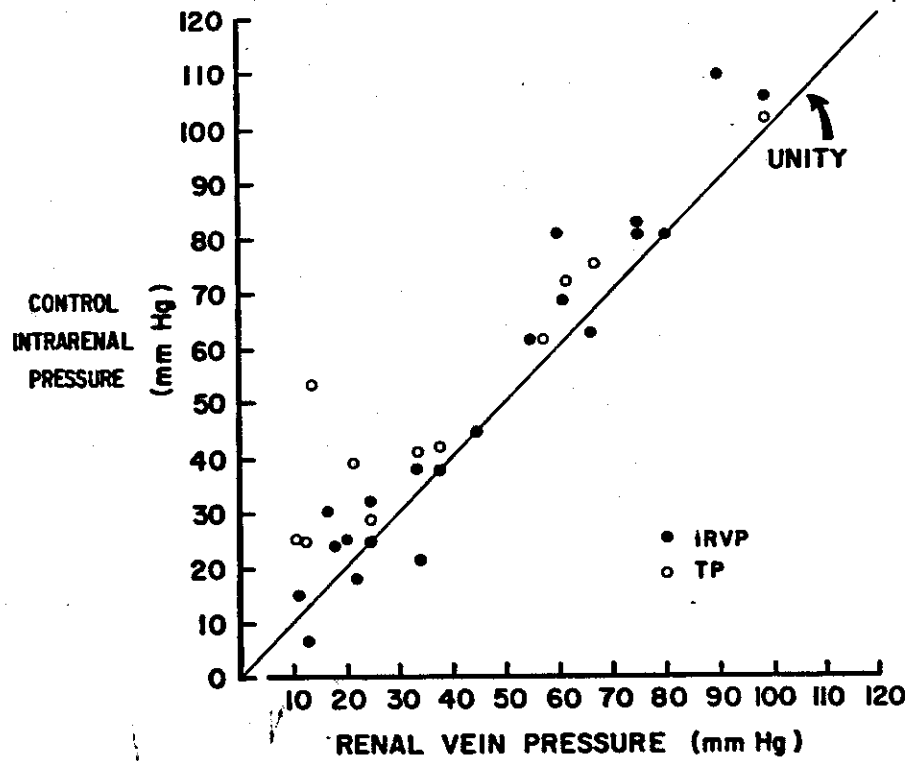


FIGURE 4. Relationship of elevated renal vein pressure values, at which a significant decrease in renal blood flow occurs, and pre-existing (control) tissue pressures (TP) and intrarenal venous pressures (IVP). (Sixteen heart-lung perfused kidneys)

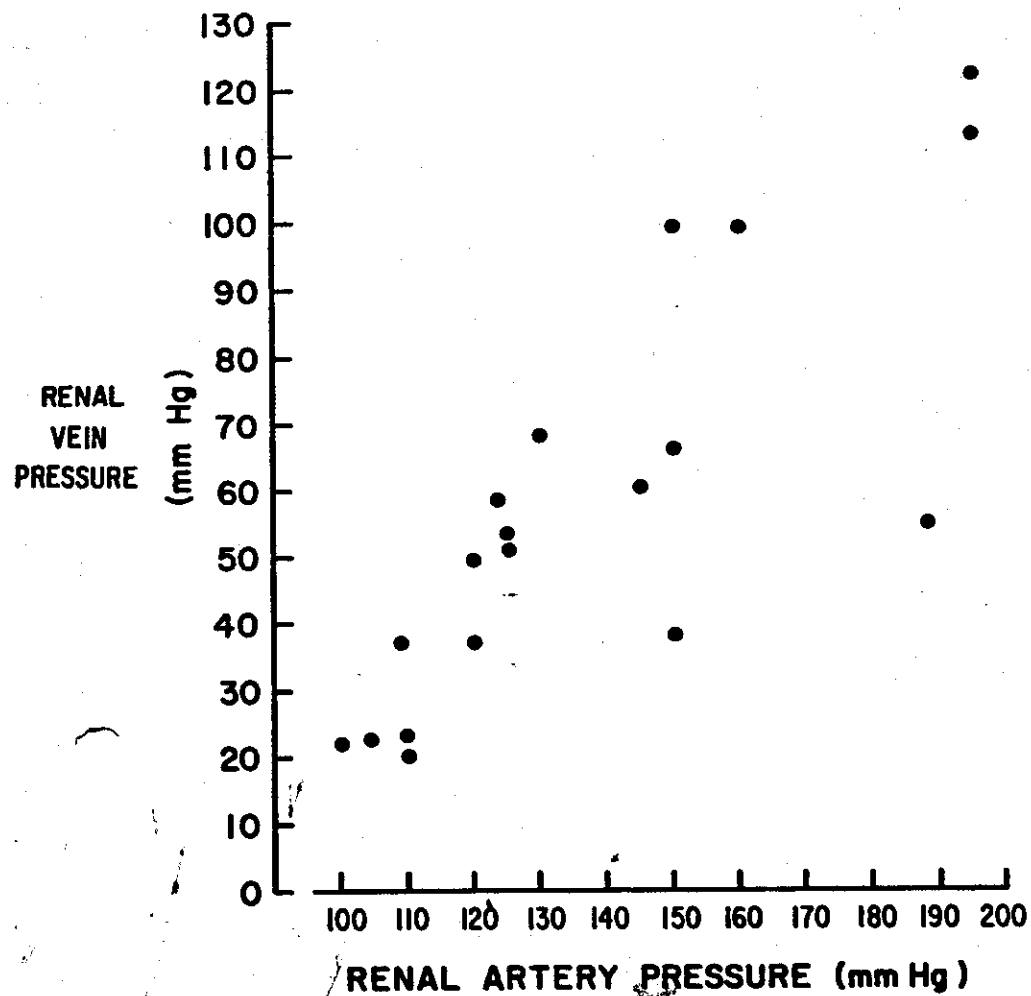


FIGURE 5. Relationship of renal artery perfusion pressure and elevated renal vein pressure values at which renal blood flow significantly falls. (Sixteen heart-lung perfused kidneys)

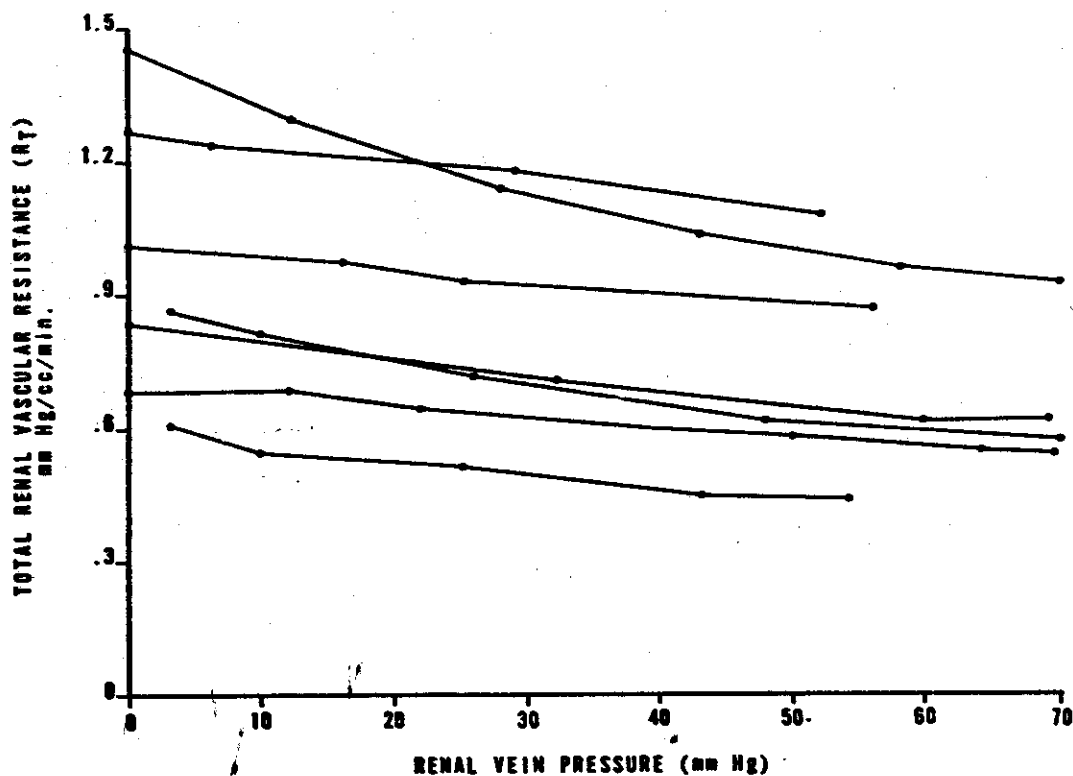


FIGURE 6. Intact innervated dog kidneys. Effect of increases in renal vein pressure on total renal vascular resistance (R_T). (7 kidneys) (kidneys perfused by intact renal artery) (Mean arterial pressure, 126 mm. Hg) (Mean control renal blood flow = 3.2 cc./min./gm.)

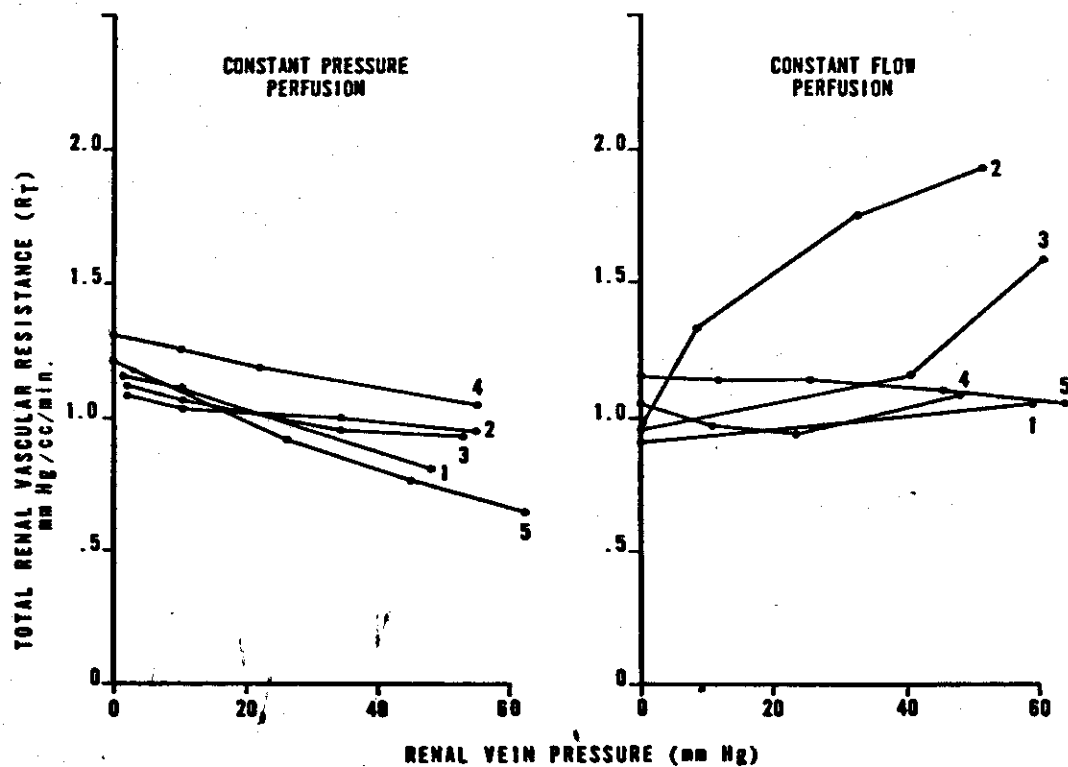


FIGURE 7. Effects of increased renal vein pressure on total renal vascular resistance in the constant flow or constant pressure perfused kidney. Results contrasted in same kidney during (a) perfusion at constant arterial inflow (Sigma-motor pump) and (b) perfusion at constant renal artery pressure (Starling shunt device) (five kidneys)

DISCUSSION

The findings from these studies assign prominent roles to intrarenal venous and tissue pressures: they appear to "buffer" the kidney against the effects of elevated renal venous pressure throughout a variable but unusually large venous pressure range. A decrease in total renal vascular resistance occurs in both isolated perfused and intact innervated kidneys when renal venous pressure is increased through a wide range. It is of interest that this decrease in resistance is primarily due to the drop in venous segment resistance (R_v) while intrarenal resistance ($R_{i..}$) remains relatively constant through a wide range of venous pressures. The effect of an increase in renal vein pressure is to distend the vascular segment from the deep intrarenal veins to the renal orifice vein. The "pressure buffering" effect of intrarenal venous and tissue pressures would appear to preserve both normal renal hemodynamics and function in the face of large increases in renal venous pressure, since intrarenal resistance remains relatively constant. It is of interest that this buffering effect is more prominent at the higher renal artery pressure range.

These findings provide evidence for the absence of a "veni-vasomotor" or "venous-arteriolar" reflex (3,6) and provide an explanation for the discrepancy of the presently reported results with those of others (3-6). This study shows that during constant flow perfusion an increase in renal vein pressure may result in an increase in total renal vascular resistance in the perfused kidney, and this has been shown by others (4,5). Since the intact kidney is not normally perfused at constant flow, this rise in resistance is apparently due to the peculiarly abnormal conditions of this technique: blood being driven through the kidney at a constant flow rate in the face of a progressively elevated renal venous pressure, results in a swollen kidney, extravascular pressure increases and intravascular pressure rises while transmural pressures remain relatively constant. Two opposing forces appear to operate during constant flow perfusion when renal vein pressure is increased:

(a) passive dilation of the venous bed and (b) compression of blood vessels by increased tissue pressure. The net effect on resistance changes depends on which force predominates. During constant pressure perfusion on the other hand, one force primarily appears to be in evidence, i.e., venous distention, and the result is a consistent decrease in resistance. Ochwald's resistance increases in the constant flow perfused kidney were very great (4). He found that increasing venous pressure to 40 mm. Hg produced an increase in resistance of approximately twice the control value. The kidneys, however, in his experiments were placed within a hermetically sealed saline filled chamber which undoubtedly resulted in exaggerated compression effects with elevated renal vein pressure at constant flow perfusion.

Urine flow changes were variable, but generally after a period of relative constancy, declined markedly. This observation is consistent with that of Winton (14) who pointed out that back-pressure effects of renal vein pressure on increasing tubular pressure may offset an increased glomerular pressure. Two opposing forces are involved in this instance and the net effect is variable, particularly with venous pressures in the lower range (0-25 mm. Hg).

The phenomenon of renal autoregulation (i. e., the tendency for renal blood flow to change less than expected through a wide arterial pressure range), may be extended on the basis of the present study, to include a similar phenomenon operating at the venous end of the renal circulation: there is a fairly constant renal blood flow through a wide range of renal venous pressures. The findings of the present study provide corroborative support for the tissue pressure theory of renal autoregulation (9, 10, 13), and suggest that a pre-venous myogenic reflex resulting from venous distention, is not operative in the kidney. From the results of this and other studies (10, 11), intrarenal resistance ($R_{i..}$) appears to be relatively uninfluenced through large increases in both renal artery and renal vein pressures.

It is of interest to consider the physiological implications of these findings as they relate to

Effects of increased renal vein pressures result from postural or body positional changes in congestive heart failure (7).

These results indicate that at normal renal vein pressures, renal vein pressure may be elevated to considerably high levels before any hemodynamic renal alterations occur. Changes in body position or posture would be tolerated very well in this instance with no adverse effects on the kidney due to venous congestion. Serious difficulties may arise under conditions of shock or hypotension when renal artery pressure is depressed or when renal arterial vasoconstriction has occurred. Rather small changes in renal venous pressure would in these latter instances, be expected to have detrimental or depressant effects on renal hemodynamics and function.

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