Redistribution of Renal Cortical Blood Flow During Ureteral Occlusion and Renal Venous Constriction[1] (35918)

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We have demonstrated that reduction in renal arterial pressure results in redistribution of renal blood flow from the outermost cortex to the deeper cortex areas (1). An identical pattern of redistribution has also been observed during the administration of acetylcholine directly into the renal artery (2). Since the redistribution is caused by both pressure reduction and vasoactive drugs, it probably represents differences in the responsiveness of the cortex zones to vasodilator stimuli of any type.

It has been observed that ureteral occlusion can result in an increase in renal blood flow (3–11). This response, like the renal vascular response to decreased renal arterial pressure (12), is associated with afferent arteriolar vasodilation (10, 13). In addition, renal venous constriction during oliguria is associated with constancy of renal blood flow (14, 15) and glomerular filtration rate (15). This observation also indicates afferent arteriolar vasodilation. A redistribution of renal cortical blood flow would be expected during ureteral occlusion and renal venous occlusion if these maneuvers cause renal vascular responses, which are qualitatively similar to those during reduction of renal arterial pressure, as suggested by the evidence cited above. Previous work on this subject is scanty. The results obtained using the inert gas washout technique have suggested that ureteral occlusion causes no redistribution of blood flow between outer cortex and juxtamedullary cortex during saline diuresis (8). The purpose of the present experiments was to apply the microsphere method to determine whether these maneuvers cause an intrarenal distribution of blood flow similar to that produced by decreased renal arterial pressure.

Methods. Mongrel dogs ranging in weight from 14 to 24 kg were anesthetized with intravenous pentobarbital, 25 mg/kg. The urinary bladder was catheterized. The left kidney was exposed via a retroperitoneal flank incision; and all visible nerves entering the renal hilum were divided. The left ureter was cannulated; and urine flow was measured by a drop counter or timed collections, depending on flow rate. Ureteral occlusion was performed by connection of the ureteral cannula to a Statham P23G pressure transducer. An adjustable clamp was placed around the aorta cephalad to the renal artery to permit manipulation of renal arterial pressure. In one series of experiments, an adjustable ligature was placed around the left renal vein to permit elevation of renal venous pressure. Pressure in the renal vein proximal to the ligature was measured via a cannula inserted into the renal vein through the left spermatic or ovarian vein. Total renal blood flow (RBF) was measured by an electromagnetic flowmeter (Medicon K-4000). Zero flow base line was determined by brief occlusion of the renal artery distal to the flow probe. Flow probes were calibrated by saline perfusion of excised vessels. Renal arterial pressure was considered equal to aortic pressure measured at the level of the renal artery via a left femoral arterial cannulation. Renal blood flow, ureteral pressure, and renal arterial pressure were recorded continuously by a Beckman R dynagraph.

The distribution of cortical blood flow was determined using radioactive microspheres

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TABLE I. Mean Values of Renal Arterial Pressure and Renal Blood Flow During Each Experimental Period for the Four Experimental Protocols.[a]

	Renal arterial pressure (mm Hg)		Renal blood flow (ml/100 g min)	
	Mean	SE	Mean	SE
Saline series, $N = 6$				
Control	135	3	373	44
Aortic constriction	78	5[d]	358	38
Diuresis	131	8	409	27
Diuresis + ureteral occlusion	136	6	618	67[d]
Mannitol series, $N = 10$				
Control	131	5	389	51
Aortic constriction	77	4[d]	387	49
Diuresis	134	4	511	67[c]
Diuresis + ureteral occlusion	139	5	517	76[b]
Ethacrynic acid series, $N = 7$				
Control	134	4	456	25
Aortic constriction	76	6[d]	446	28
Diuresis	136	4	783	46[d]
Diuresis + ureteral occlusion	135	2	657	62[b]
Renal venous constriction series, $N = 10$				
Control	142	4	375	34
Aortic constriction	76	3[d]	376	37
Venous constriction	139	3	370	37

[a] All values presented as mean ± standard error. The significance of difference from control values are indicated as follows: [b] $p < .05$; [c] $p < .01$; [d] $p < .001$.

(3M Company, St. Paul, MN) according to a technique described in an earlier publication (1). Briefly, a suspension of plastic microspheres 19 μ in diameter was injected into the left ventricle through a catheter introduced via the left carotid artery. Each injection contained 0.5 mg of bead mass, representing approximately 95,000 microspheres. Sequential injections were performed using microspheres labeled with different gamma emitting isotopes. Four cortex zones of equal thickness were analyzed for individual isotope content (16) and perfusion rate of each zone calculated. Time (up to 1 hr) and repeated embolization (up to four times) have been shown to have no effect on the cortical distribution of microspheres (1).

Experimental protocols. There were four experimental protocols; venous constriction and ureteral occlusion during three different types of diuresis. In each series, the first microsphere injection was made in the absence of any manipulation or intervention (control). Subsequently the aortic clamp was tightened to reduce renal arterial pressure to the lowest level at which renal blood flow remained constant, following which the second microsphere injection was performed. The aortic clamp was then released with an increase of renal arterial pressure to control levels. We have previously demonstrated that the flow rates of the individual cortex zones are not affected by a prior temporary reduction in renal arterial pressure (1). In the renal venous constriction series (10 expts.), the renal vein was then constricted to produce the highest renal venous pressure at which renal blood flow remained constant. Under this condition, a third injection of microspheres was performed.

Saline diuresis (6 expts.) was induced by a loading infusion of 20 ml/kg of 0.85% saline followed by a maintenance infusion of 0.7 ml/kg min. Ethacrynic acid diuresis (7 expts.) was induced by intravenous administration of Edecrin, Merck, 2 mg/kg, followed

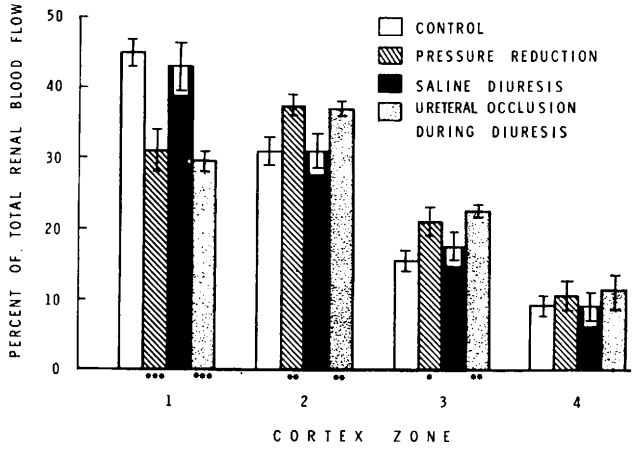

FIG. 1. Distribution of cortex blood flow during the four experimental periods of the saline diuresis protocol; asterisks indicate significance of difference from control: $*p<.05$; $**p<.01$; $***p<.001$.

by a maintenance infusion of 2 mg/kg hr. To maintain approximate overall fluid and electrolyte equilibrium, normal saline was infused intravenously at a rate continuously matched to total urine flow. Hypertonic mannitol diuresis was induced by infusion of a solution of mannitol (Fisher Scientific Co.) in normal saline with a concentration of 15 g/100 ml final volume. The infusion rate was 0.7 ml/kg min. In each diuretic series, urine flow and renal blood flow became relatively stable 30 min after starting the maintenance infusion. At this time, a third injection of microspheres was performed. The ureter was then occluded acutely by diversion of the ureteral cannula into a pressure transducer. Ureteral pressure rose quickly, reaching a plateau in less than 20 min. A fourth injection of microspheres was then performed.

Analysis of results. The distribution of cortex blood flow as analyzed by calculation of the percentage of total renal blood flow perfusing the individual cortex zones (1). This expression takes into account both the perfusion of each cortex zone and its mass as a percentage of the renal cortex. Changes in zonal flow distribution reflect changes in relative flow rates of the individual cortex zones, since the tissue masses to which the flows were referred were constant for a given kidney under all experimental conditions. Statistical significance was assessed by the *t* test or paired *t* test as appropriate (17).

Results. Overall renal hemodynamic data from the four experimental series are presented in Table I. There was no difference between the series in terms of control renal arterial pressure or renal arterial pressure during aortic constriction. The arterial pressure during aortic constriction was significantly less than control in each series. Neither the ureteral or venous occlusion procedures had an effect on renal arterial pressure. There was no significant difference between the series in control renal blood flow or renal blood flow during aortic constriction. The diuretic procedures produced differing effects on renal blood flow. Saline diuresis was without significant effect while both mannitol and ethacrynic acid diuresis resulted in significant increases in total renal blood flow. The renal blood flow effect of ureteral occlusion also depended on the type of associated diuresis. Ureteral occlusion produced a significant increase in renal blood flow during saline diuresis, no effect during mannitol diuresis, and an insiginficant decrease during ethacrynic acid diuresis. Interestingly, the net result on renal blood flow of combined diuresis and occlusion was an increase of similar magnitude in all three groups.

The urine flow during control periods did not differ between the groups. The mean for all series was 1.29 ± 0.32 ml/100 g min. The urine flow during the various diuretic conditions were: saline diuresis 11.4 ± 2.8 ml/100 g min, mannitol diuresis 12.4 ± 1.6 ml/100

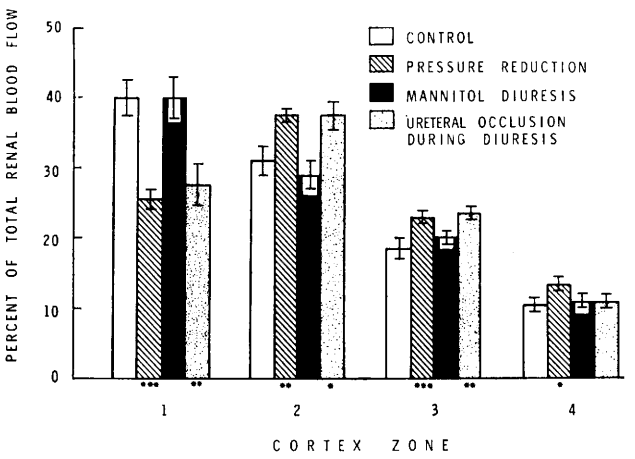

FIG. 2. Distribution of cortex blood flow during the four experimental periods of the mannitol diuresis protocol; asterisks indicate significance of difference from control: * $p<.05$; ** $p<.01$; *** $p<.001$.

g min, and ethacrynic acid diuresis 35 ± 4.3 ml/100 g min.

Occluded ureteral pressure was significantly ($p<.05$) higher during mannitol diuresis (80.8 ± 4.7 mm Hg) than during saline diuresis (64.2 ± 4.2 mm Hg). The ureteral pressure during ethacrynic acid diuresis (72.4 ± 5.5 mm Hg) was intermediate between saline diuresis and mannitol diuresis and not significantly different from either.

The effects of the various maneuvers on intrarenal distribution of blood flow are presented in Figs. 1–4. Decreased renal arterial pressure produced essentially the same effect on cortical blood flow in all series, *i.e.*, a redistribution of flow from the outermost cortex to deeper cortex zones. In Table II, we present the pooled data from all four groups in terms of percentage of total renal blood flow perfusing each cortex zone at normal and reduced arterial pressure. Pressure reduction caused a significant increase in the percentage flow perfusing cortex zones 2, 3, and 4. When the four experimental groups were analyzed individually (Fig. 1–4), the change in percentage distribution to cortex zone 4 was significant for only the mannitol and venous constriction series.

Neither saline diuresis nor mannitol diuresis had any effect on the intrarenal distribution of blood flow. However, ethacrynic acid diuresis resulted in flow redistribution from cortex zone 1 to cortex zones 2 and 3, an observation documented earlier in this laboratory (2). The effect of ureteral occlusion on cortex blood flow distribution is presented in Table III. The findings depended on the type of diuresis. There was a significant redistribution during both saline diuresis and mannitol diuresis. However, ureteral occluson during ethacrynic acid diuresis had no effect on the intrarenal distribution of blood flow.

In each diuretic state, the cortical blood

TABLE II. Percentage of Total Blood Flow per Cortex Zone ($N = 33$).

Cortex zone:	1		2		3		4	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Control RAP[a]	41.3	1.3	31.4	1.5	18.1	0.7	9.3	0.6
Reduced RAP	26.6	1.2[b]	37.3	0.7[b]	23.9	0.7[b]	12.4	0.7[b]

[a] RAP = renal arterial pressure.

[b] Signifies that the value during decreased RAP differs from that during control RAP with a significance $p < .001$.

TABLE III. Effect of Ureteral Occlusion on the Distribution of Cortex Blood Flow, Calculated as Percentage of Total Cortex Flow During Ureteral Occlusion Minus Percentage of Total Cortex Flow During Diuresis.[a]

Cortex zone:	1	2	3	4
Experimental series				
Saline diuresis $N = 6$	−13.8 ± 3.4[c]	6.3 ± 1.7[b]	5.2 ± 2.6	2.5 ± 2.1
Mannitol diuresis $N = 10$	−12.3 ± 3.4[c]	8.4 ± 2.9[b]	3.4 ± 1.1[b]	0.2 ± 0.6
Ethacrynic acid diuresis $N = 7$	−2.8 ± 1.7	0.4 ± 1.7	1.9 ± 1.2	0.4 ± 1.4

[a] All values expressed as mean ± standard error.
[b] Signifies: $p < .05$; [c] $p < .01$.

flow distribution during ureteral occlusion closely resembled that during decreased renal arterial pressure. Thus, during saline diuresis and mannitol diuresis redistribution occurred in the same pattern as observed during decreased renal arterial pressure, *i.e.*, a shift from cortex zone 1 to cortex zones 2 and 3. During mannitol diuresis there was a slightly lesser percentage flow to cortex zone 4 (2.7 ± 0.7%, $p<.01$) than during pressure reduction. Since cortical blood flow distribution during ethacrynic acid diuresis prior to ureteral occlusion closely resembled that during decreased renal arterial pressure (Fig. 3), the net effect of combined ureteral occlusion and ethacrynic acid diuresis was a pattern, which also closely resembled that during decreased renal arterial pressure. The only difference was a slightly lesser percentage (3.1 ± 1.1, $p<.05$) of flow to cortex zone 4 during ureteral occlusion than during pressure reduction.

Renal venous pressure during control periods was 7.9 ± 0.9 mm Hg, and during venous constriction 62.2 ± 3.8 mm Hg. Renal venous constriction had no effect on total renal blood flow or renal arterial pressure (Table I), but caused a significant redistribution of blood flow from cortex zone 1 to cortex zones 2, 3 and 4 (Fig. 4). This redis-

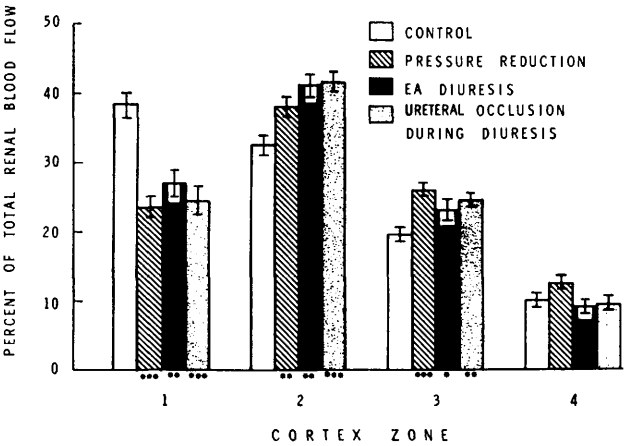

FIG. 3. Distribution of cortex blood flow during the four experimental periods of the ethacrynic acid diuresis protocol; asterisks indicate significance of difference from control: * $p<.05$; ** $p<.01$; *** $p<.001$.

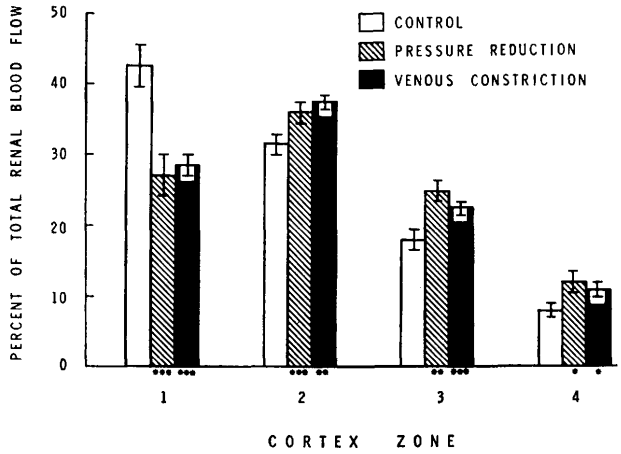

FIG. 4. Distribution of cortex blood flow during the three experimental periods of the venous constriction protocol; asterisks indicate significance of difference from control: * $p<.05$; ** $p<.01$; *** $p<.001$.

tributional pattern was identical to that observed during reduction in renal arterial pressure.

Discussion. Our observations concerning the effect of ureteral occlusion on total renal blood flow are in accord with those from the literature. It is noteworthy that the effect of ureteral occlusion depends on the type of accompanying diuresis. We found that saline infusion *per se* had no significant effect on renal blood flow and that ureteral occlusion during saline diuresis caused an increase in renal blood flow (3–5, 8, 9). In contrast, mannitol diuresis was associated with an increase in blood flow but ureteral occlusion during mannitol diuresis had no further effect on renal blood flow (6–8). The ethacrynic acid diuresis was associated with a third pattern characterized by a larger increase in renal blood flow than was produced by mannitol ($p<.01$) and a decrease in renal blood flow during ureteral occlusion. The effect of ureteral occlusion on renal blood flow during ethacrynic acid diuresis may reflect the demonstrated effect of ethacrynic acid to abolish renal autoregulation (18). It has been observed that, in the absence of autoregulation, ureteral occlusion causes a decrease in renal blood flow (4).

Ureteral occlusion was found to cause a redistribution of cortex blood flow from cortex zone 1 to cortex zones 2 and 3. The magnitude of the distribution was relatively large, being 13.8 and 12.3% of total renal blood flow in saline diuresis and mannitol diuresis, respectively. The redistribution was not dependent on the effect of ureteral occlusion to increase renal blood flow since during mannitol diuresis ureteral occlusion produced no effect on renal blood flow. In contrast to the effect of ureteral occlusion during saline and mannitol diuresis, there was no change in the distribution of blood flow when the ureter was occluded during ethacrynic acid diuresis. It is noteworthy that ethacrynic acid diuresis also differed from saline and mannitol diuresis in causing a redistribution of cortical blood flow in the absence of ureteral occlusion. These two differences are probably related. The pattern and magnitude of cortical blood flow redistribution during ethacrynic acid diuresis was virtually identical to that caused by pressure reduction. Both conditions are characterized by near maximal renal vasodilation and passive pressure-flow relationships as pressure is further reduced (18). It is plausible that this pattern reflected a maximum capacity for vasodilation by the renal vascular segments responsible for redistribution, and that no further effect could be elicited in response to ureteral occlusion. It is pertinent, in this regard, that reduction in renal arterial pressure below the autoregulatory range does not cause greater redistribution of cortex blood flow than does reduction to the lower autoregulatory limit (1).

It seems likely that the presence of a high pressure in the renal pelvis was not *per se* a factor influencing blood flow distribution, since ureteral occlusion during ethacrynic acid diuresis did not cause a change in the distribution of flow from that seen during ethacrynic acid diuresis prior to ureteral occlusion.

The pattern of redistribution observed during venous constriction was identical to that produced by ureteral occlusion. Since venous constriction was only performed in oliguric animals the flow distribution did not depend on the presence of a diuresis.

Comparison of the distribution of cortex blood flow during ureteral occlusion and renal venous constriction with that observed during decreased renal arterial pressure revealed a virtually indistinguishable pattern of redistribution from superficial to deep cortex. It is clear that reduction in renal arterial pressure causes afferent arteriolar tone to decrease to a physiological minimum (12). The observation that glomerular filtration rate does not decrease during elevation of ureteral pressure to 55 mm Hg (10) or elevation of renal venous pressure to 40 mm Hg (15) may be interpreted as evidence that afferent arteriolar resistance has declined. Navar (13) concludes that afferent resistance reaches a physiological minimum during ureteral occlusion. The similarity of patterns in flow redistribution would be consistent with the idea that responses of the afferent arteriolar resistance may be virtually identical in the various cortex zones of the kidney during ureteral occlusion, venous constriction, and reduction in renal arterial pressure.

The principle feature common to both ureteral occlusion and renal venous constriction is an elevation of pressure in the peritubular capillaries (19) which presumably reflects renal interstitial pressure. Both maneuvers would therefore tend to decrease arteriolar transmural pressure. A similar effect is produced by a decrease in renal arterial pressure. The similar distributional effects of ureteral occlusion, venous constriction, and pressure reduction suggest that all three adaptations may depend on a myogenic response to changes in arteriolar transmural pressure.

Our observations are not directly comparable with previous studies of renal blood flow distribution during ureteral occlusion (3, 8) since, in those studies, cortex blood flow was not analyzed in four discrete zones as we have done (3, 8). It has been inferred from changes in E_{PAH} that medullary blood flow increases during ureteral occlusion (5), and this conclusion has been reached independently using tissue measurements of transit time of intravascular dye (3). Our data do not bear on this problem since the microsphere method does not permit measurements of the post glomerular renal circulation, due to the fact that virtually all microspheres of the size which we injected are arrested in the glomerular capillaries. However, to the extent that medullary blood flow arises from glomeruli located in the inner two cortex zones, an increase in medullary blood flow would be consistent with redistribution to cortex zone 3 observed during ureteral occlusion.

Summary. The distribution of blood flow between four zones of the canine renal cortex was measured by the tracer-labeled microsphere technique. The effect of ureteral occlusion on cortex zone flow distribution was studied during saline diuresis, mannitol diuresis, and ethacrynic acid diuresis. Renal venous constriction was performed in oliguric animals. The venous pressure was elevated to an average of 62.2 mm Hg, the highest level at which renal blood flow remained constant. Both ureteral occlusion and renal venous constriction resulted in a redistribution of flow from the most superficial cortex to deeper cortex zones. We infer that the redistribution reflects the renal circulatory response to elevated renal interstitial pressure since it was produced by both renal venous constriction and ureteral occlusion and was independent of the type of accompanying diuresis. This redistribution was found to be indistinguishable from that caused by reduction in renal arterial pressure. This suggests that a common mechanism accounts for the intrarenal circulatory responses to decreased perfusion pressure and increased renal interstitial pressure.

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