Mechanisms of Autoregulation in Isolated Perfused Kidney.* (25524)

LERNER B. HINSHAW† AND CURTIS H. CARLSON
Depts. of Physiology and Physiological Chemistry, University of Minnesota, Minneapolis

The important role of intrarenal extravascular pressure changes in regulation of blood flow through the kidney has been previously reported(1). The further observation that "intrarenal" vascular resistance (renal artery pressure-tissue pressure/flow) often rises with renal artery pressure elevation suggests that causative factors other than tissue pressure changes are involved in the autoregulation phenomenon(1). Among other possibilities, it has been suggested(1) that extravascular pressures within Bowman's capsule may exceed the general renal tissue pressure, resulting in a fall in glomerular transmural pressure. The effect of glomerular filtration on post-glomerular vascular resistance by virtue of changes in blood viscosity, is also to be considered as an additional factor in elevating renal vascular resistance(2,3). Autoregulation of flow is reported to occur in kidneys perfused with colloidal solutions containing virtually no red blood cells(4,5,6) and is also found in intact kidneys when the blood hematocrit is very low(7). It thus appears that blood viscosity changes cannot be solely responsible for renal flow regulation. Calculations of "intrarenal" resistance (RA-TP/F) (1) have been made in the present study in blood- and dextran-perfused dog kidneys to distinguish between relative effects of tissue pressure and post-glomerular viscosity changes on "overall" vascular resistance. The possible compression effect of Bowman capsule extravascular pressure in providing a fraction of the rise in renal vascular resistance has also been investigated.

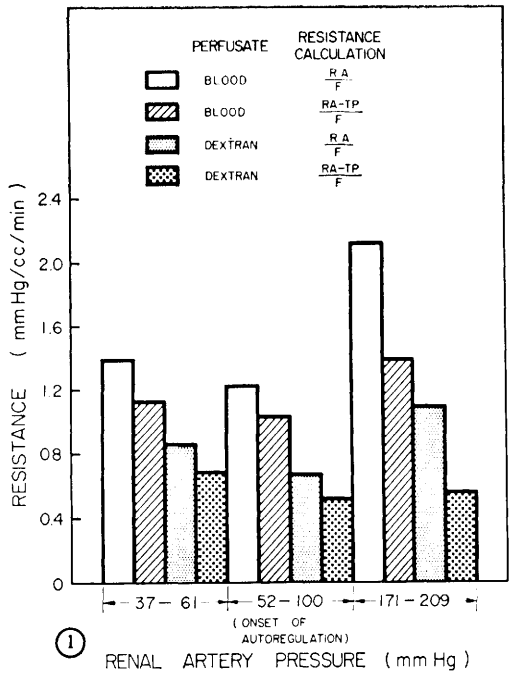
Methods. Kidneys were removed from anesthetized animals without interruption of renal blood flow and perfused at a controlled arterial presure with a pump-lung apparatus as described previously(1). In the first series of experiments isolated kidneys were alternately perfused with 4% dextran and blood as reported previously(6). Renal vein pressures were maintained at zero mm Hg. Tissue pressures and flows were determined as recently described(1,6), and "overall" (RA/F) and "intrarenal" (RA-TP/F) vascular resistances were calculated(1). In a second group of experiments isolated kidneys were perfused with blood during which time the ureters were totally occluded. Tissue and ureteral pressures were simultaneously measured as renal artery pressure was progressively elevated through the autoregulatory range. Ureteral pressures obtained in these studies were assumed to approximate the extravascular pressure in Bowman's capsule, since glomerular filtration is very low(8). All pressures were measured by means of Statham strain gauges and registered on a direct writing four channel Polyviso Sanborn recorder.

Results. Data from blood- and dextran-perfused kidneys are presented in Fig. 1. Mean values for "overall" and "intrarenal" resistances have been obtained from 14 perfusion studies. Vascular resistance calculations have been grouped into 3 renal artery pressure levels: (a) 37-61 mm Hg (prior to onset of autoregulation); (b) 52-100 mm Hg (at onset of autoregulation when all resistances are at lowest values); (c) 171-209 mm Hg (when resistances are at highest values). Although it is seen that "intrarenal" vascular resistance rises somewhat through the autoregulatory range in blood-perfused kidneys, it increases very little during the same period in dextran-perfused kidneys.

Fig. 2 depicts data obtained in a separate study when 3 isolated kidneys were perfused with blood, and ureters were continuously clamped. As renal artery pressure is progressively elevated, both tissue and ureteral pressures rise to varying degrees. Ureteral pressure is observed to increase progressively more

* Research suppcrted by grant from Graduate School, Univ. of Minn.

† Research performed during term of Lederle Medical Faculty Award, 1959-1962.



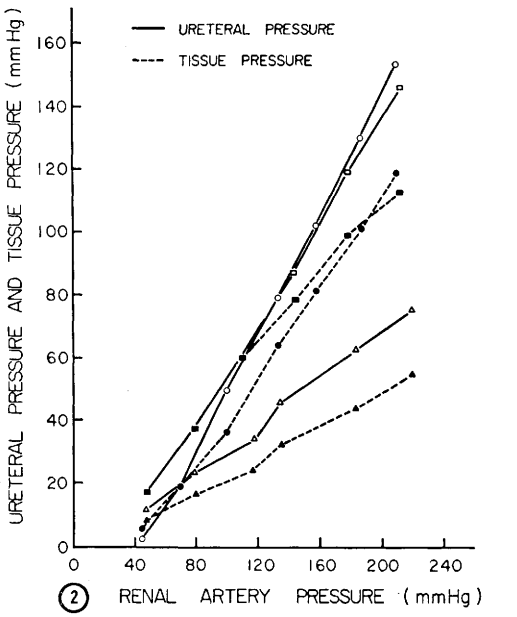


FIG. 1. Mean values of "overall" (RA/F) and "intrarenal" (RA-TP/F) vascular resistance in blood- and dextran-perfused dog kidneys. Resistances are calculated from data obtained following progressive elevation of renal artery pressure.

FIG. 2. Ureteral and tissue pressures obtained in 3 isolated blood-perfused dog kidneys during progressive elevation of renal artery pressure (ureters continuously clamped). Solid and open symbols refer to tissue and ureteral pressures, respectively, with identically-shaped symbols representing each separate kidney perfusion.

rapidly than tissue pressure as arterial pressure is elevated.

The 3 factors considered responsible for autoregulation in the isolated perfused kidney are illustrated in Fig. 3 and approximate fractional roles of each have been assigned. The increment in resistance due to excess of Bowman capsule extravascular pressure over general tissue pressure has been designated as "Bowman capsule pressure."

Discussion. The present study was designed to evaluate the relative effects of factors considered responsible for the autoregulation phenomenon. Findings suggest that blood flow regulation in the isolated perfused kidney is brought about by (a) the combined effects of extravascular pressures within and without Bowman's capsule and (b) changes in blood viscosity resulting from glomerular filtration. The latter factor is considered to be extremely variable, depending on intrarenal hematocrit and glomerular filtration rate(2, 10). Although other factors may perform additional roles in increasing resistance, in view of the present data, their effects need not be included to account for the phenomenon of autoregulation.

In contrast to the observations of Malvin and Wilde(8), renal blood flow was markedly decreased following occlusion of the ureter, as was also reported by Winton(9). Autoregulation of blood flow occurred to a high degree during continuous occlusion of the ure-

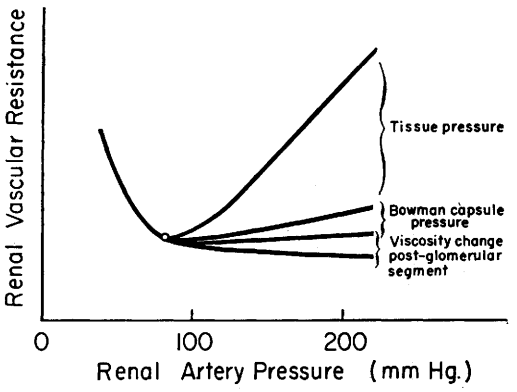


FIG. 3. Relative approximate roles of changes in tissue pressure, Bowman capsule extravascular pressure and post-glomerular blood viscosity on renal vascular resistance in the isolated perfused dog kidney.

ter, although estimations of pre-glomerular resistance showed no rise throughout the autoregulatory period. The observation that ureteral pressure is greater than tissue pressure suggests that Bowman capsule extravascular pressure is an effective compressing force on the renal vascular bed. These data also suggest that tubules possess considerable structural rigidity.

Mechanisms of autoregulation, according to the present study, appear to operate primarily in association with glomerular filtration and also extend their effects through the post-glomerular segment. The "clamping" effect of extravascular pressure on intra-parenchymal arterial vessels has not been evaluated.

Summary. The present investigation has been concerned with mechanisms explaining autoregulation of renal blood flow. Data from experiments on the isolated perfused dog kidney suggest that as renal artery pressure is elevated, blood flow regulation is brought about by (a) combined effects of increased tissue pressure and Bowman capsule extravascular pressure, and (b) increases in post-glomerular viscosity resulting from glomerular filtration.

1. Hinshaw, L. B., Day, S. B., Carlson, C. H., *Am. J. Physiol.*, 1959, v197, 309.
2. Winton, F. R., *Trans. Third Conf. on Renal Function, N. Y.*, Macy, 1952, 51.
3. Selkurt, E. E., *Am. J. Physiol.*, 1946, v147, 537.
4. Waugh, W. H., *Circ. Res.*, 1958, v6, 363.
5. Weiss, C., Passow, H., Rothstein, A., *Am. J. Physiol.*, 1959, v196, 1115.
6. Hinshaw, L. B., Ballin, H. M., Day, S. B., Carlson, C. H., *ibid.*, 1959, v197, 853.
7. Thompson, D. D., Kavaler, F., Lozano, R., Pitts, R. F., *ibid.*, 1957, v191, 493.
8. Malvin, R. L., Wilde, W. S., Sullivan, L. P., *ibid.*, 1958, v194, 135.
9. Winton, F. R., *Harvey Lectures*, N. Y., Academic Press, 1951-52, 21.
10. Whittaker, S. R. F., Winton, F. R., *J. Physiol.*, 1933, v78, 339.

Received December 3, 1959. P.S.E.B.M., 1960, v103.

Influence of Sodium Thiosulfate on Reducing Capacity of Human Erythrocytes *in vivo*.* (25525)

HOWARD S. SCHWARTZ,† BARUCH LANDAU‡ AND LOUIS J. SOFFER
Endocrine Laboratory and Dept. of Medicine, Mount Sinai Hospital, N. Y. City

Ability of the red blood cell to reduce iodine is, to a great extent, a function of its glutathione content(1). We observed that, during intravenous infusion of sodium thiosulfate, there occurs a diminution in reducing capacity of red blood cells. We established an index determined by the ratio between this diminution and amount of sodium thiosulfate infused. Erythrocytes of normal women had a reductivity index (R.I.) which was more than double that of normal men.

Method. One hundred ml of 10% $Na_2S_2O_3 \cdot 5\ H_2O$ was infused intravenously as described by Cardozo and Edelman(2). Average duration of infusion was 10 minutes. Venous blood was withdrawn in heparinized syringes at 0, 25, 35, 45, and 60 minutes after beginning of infusion. Each blood specimen was divided into 2 portions. The first part was used for iodimetric titration of whole blood, the second portion for iodimetric titration of serum(3). Volume of iodine used for each titration is employed to determine reducing capacity of the sample at each time interval and is measured in terms of arbitrarily devised reductivity units (r.u.). Ten r.u. are equal to that volume of N/1000 iodine standard required to titrate 0.5 mg of sodium thiosulfate standard. The N/1000 iodine solution was prepared from N/10 iodine(4) by dilution. One g KI/100 ml was then added to stabilize final solution as recommended by

* Aided by grant from Muscular Dystrophy Assn.
† Trainee, NIH, Inst. of Arthritis and Metabolic Dis.
‡ Dazian Fellow.