Effect of Elevation of Intraluminal Pressure on Renal Vascular Resistance

By Francis J. Haddy, M.D., Ph.D.

With Collaboration of Jerry Scott and Edwin Armstrong

Elevation of renal venous pressure in pentobarbitalized laparotomized dogs elicits renal vascular constriction. Part of this constriction appears to be dependent upon a venous-arteriolar reflex. The reflex pathway is not distributed locally. A portion of this reflex appears to be dependent upon still unrecognized factors.

BURTON and colleagues suggested recently that stretching the venous wall in limbs elicits a local reflex resulting in constriction of local arteriols. They felt that this "veni-vasomotor" reflex supplemented the central buffer reflexes in controlling blood flow through extremities during change in posture. Utilizing methods permitting direct measurement of small and large vessel resistance in the dog foreleg, Haddy and Gilbert independently reached a similar conclusion, except they felt the reflex was not necessarily local.

The present study was carried out to determine whether a venous-arteriolar reflex is present in the dog kidney. The study appeared to have special interest since the presence of such a reflex might influence effective filtration pressure and thereby urine flow rate in conditions characterized by venous hypertension.

Methods

Twenty-eight mongrel dogs were anesthetized with sodium pentobarbital. With the animal on the left side, the right kidney was exposed through a right flank incision. In the first series of experiments, the renal artery and vein were dissected free near the aorta and vena cava respectively. Blunt dissection was employed throughout in order to preserve as many nerve fibers as possible. In the second series of experiments, the kidney was denervated completely by meticulously removing all nerve fibers and other tissue from the artery, vein, ureter, hilar area and kidney substance. Two per cent procaine was poured on the artery and vein in order to block any microscopic fibers not interrupted by gross dissection. A suture was looped loosely around the renal vein near the vena cava. The animal was heparinized. The femoral artery was connected to the renal artery with a length of polyethylene tubing which coursed through a variable flow pump. Twenty-two gauge needles were inserted in the renal artery and vein. Pressures in these vessels were measured utilizing a 0–75 cm. Hg resistance wire pressure transducer.

The first phase of the study was directed at determining the effect of elevation of arterial and venous transmural pressures on the geometric component of resistance. The renal artery blood flow was maintained constant while the ligature around the renal vein was tightened progressively. Change in renal vein pressure from the control value was used as a guide to the degree of obstruction produced. Renal vein pressure was elevated in increments of 5 mm. Hg until the total elevation equaled 25 mm. Hg. Pressure was measured in the renal artery and vein at each increment in flow after waiting a few seconds for transient changes to disappear. Not more than 5 min. elapsed from the first to the last measurement.

In the first experiment, where flow was maintained constant throughout, the average change in gradient from renal artery to vein was subjected to a sta-
RESULTS

Figure 1 presents the effect of gradual renal venous obstruction upon renal arterial and venous pressures with constant renal blood flow rate. The initial and final pressure gradients also are presented. It will be noted that an elevation of renal vein pressure of 25 mm Hg was associated with a 40 mm Hg rise in renal artery pressure. This 15.0 ± 4.2* mm Hg elevation of gradient (p = <.01) represents active vasoconstriction. The rise in resistance occurred immediately upon elevation of venous pressure and remained elevated as long as venous compression was maintained. This latter period varied between a few seconds and 10 min.

* Mean ± standard error.

Figure 2 presents the effect of gradual renal vein obstruction on renal artery and vein pressures with blood flow rate constant. Elevation of renal vein pressure by 25 mm Hg was associated with only a 22 mm Hg rise in renal artery pressure. The change in gradient between initial and final conditions was -8.0 ± 1.9 mm Hg. Therefore, vascular resistance failed to rise when transmural pressure was elevated in the denervated kidney. The difference between the above gradient changes in the innervated and denervated kidneys is highly significant statistically; the t and p values being 4.05 and <0.01 respectively. The absence of a rise in resistance following section of the renal nerves indicates that the constriction observed in the intact kidney is based, at least partially, upon a nervous...
mechanism whose pathways course outside of the kidney substance.

Table 1 shows that the resistance response to elevation of arterial but not venous pressure is the same in innervated and denervated kidneys. Through the first three steps of pump acceleration, arterial pressure rose more than 50 mm. Hg whereas venous pressure rose only 3 mm. Hg. Pump acceleration over this range, then, provides a method for preferentially increasing arterial intraluminal pressure in the presence of a relatively constant venous pressure. The changes in resistance from one step to another are not significantly different in the innervated and denervated preparations. Neither were the slopes of pressure flow curves, constructed from the 2 groups of figures under consideration, significantly different. Therefore, resistance changes based upon nervous mechanisms were not demonstrated when arterial but not venous intraluminal pressure was elevated. By inference, then, the receptors responsible for the active change in vessel caliber observed in the first experiment most likely lie in the veins.

The data in Table 1 also suggest that the vascular bed of the kidney is distensible when pressure is raised on the arterial side. Associated with the first three increments in arterial pressure and flow rate was a resistance decrease in every kidney tested. Assuming a negligible role for anomalous viscosity, this resistance change indicates passive vasodilatation. The vessels of the nerve sectioned and nerve intact kidney appear to be equally distensible since the changes in resistance between each increment in arterial pressure are not significantly different. The absolute values for resistance at each arterial pressure level are also not significantly different. The latter comparison, however, may not be valid since observations were not made in the same innervated and denervated kidney.

The fact that resistance did not continue to decrease with further increments in renal artery pressure may indicate that the distention limit of either the vessels and/or the renal capsule had been reached. Of particular interest were 3 innervated and 5 denervated kidneys in which resistance actually increased over the last 3 steps. Associated with this was a rising venous pressure. Among the mechanisms which might account for the resistance rise are activation of a local venous-arteriolar reflex, the occurrence of turbulent flow and changes in the concentrations of metabolites subsequent to increasing flow rates.

Another observation which suggested the presence of a local component of the reflex was the absence of a resistance change following elevation of venous and arterial pressure in the denervated kidney (fig. 2). The absence of a resistance decrease infers some active small vessel constriction since the large vessels undoubtedly dilated passively as pressure was elevated. Further, elevation of arterial pressure alone (Table 1) indicates that the renal vascular system can be passively distended under certain conditions. Some local mechanism likely was activated to prevent distention when venous pressure also was elevated in the denervated preparation. In an attempt to ascertain the role of locally distributed sympathetic nerves in the above phenomena, the first experiment was repeated in 6 denervated kidneys following injection of various sympatholytic and adrenolytic agents (Benedriane 40 mg., regitine 5-15 mg., dibenzyline 100 mg.) into the renal artery. The average renal artery to vein gradient prior to venous
obstruction was 92 mm. Hg. Following elevation of renal vein pressure by 25 mm. Hg, the average gradient was 91 mm. Hg. These results are not different from those obtained in the denervated kidney. Further, the same maneuver in 8 nerve intact kidneys into which 5 ml. of 2 per cent procaine had been injected through the renal artery yielded initial and final pressure gradients of 78 and 83 mm. Hg respectively. Therefore, these procedures failed to demonstrate a local sympathetic component of the reflex. They do not, however, eliminate the possibilities of parasympathetic inhibition in locally distributed ganglia, pressure sensitive constrictor mechanisms located in the vascular smooth muscle itself, the unlikely possibility of a rise in extramural pressure dependent upon edema formation and mechanisms as yet unknown.

DISCUSSION

The experiments reported show that elevation of renal vein pressure elicits immediate renal vascular constriction. The vasoconstriction is partially dependent upon a nervous reflex whose pathway courses outside of the kidney substance. A portion of the vasoconstriction appears to be dependent upon still undetermined local factors. In the extremity, the mechanism, through arteriolar constriction, maintained an unchanged total resistance despite passive venous and arterial dilatation attributable to a rise in transmural pressure. By contrast, in the kidney, the mechanism overcorrected passive changes in vascular geometry resulting in a higher resistance with elevated than with normal venous pressure.

A review of the literature failed to reveal other studies concerned primarily with the effect of variations in transmural pressure on vascular resistance in the intact kidney. However, Selkurt and associates reported that elevation of renal venous pressure either caused no change or a rise in renal vascular resistance. Though not interpreted as such, these results are those expected in the presence of a venous-arteriolar reflex.

It is of interest to speculate upon the utility of a mechanism which increases renal vascular resistance upon elevation of renal venous pressure. Such a mechanism might correct resistance and blood flow changes occurring as a result of variation in intraluminal pressure during change in body position. However, the fact that the mechanism actually overcorrects these passive changes suggests yet another function. It has been shown in the human that assumption of an upright position results in reduction of renal plasma flow, glomerular filtration rate and urinary excretion of sodium and water. Similar changes, but in addition increased renal vascular resistance, have been reported during congestive heart failure. In animals, renal vein constriction reduces urine flow rate. Common to all these conditions is an elevated renal venous pressure. The experiments reported suggest that these changes may be the result of the action of the venous-arteriolar reflex. Such a renal response may be to the best interest of the organism since it would tend to limit the expected blood volume decrease subsequent to a general rise in systemic venous pressure.

SUMMARY

The right renal vascular system of pentobarbitalized laparotomized dogs was tested for the presence of a "veni-vasomotor" or "venous-arteriolar" reflex. Elevation of renal venous and arterial pressure with constant blood flow rate was associated with a significant immediate increase in renal vascular resistance in the innervated kidney. The same maneuver failed to produce a significant resistance change in kidneys which were denervated or denervated and injected with sympatholytic agents. Elevation of arterial but not venous pressure was associated with resistance changes which were not significantly different in innervated and denervated kidneys. These findings are interpreted as likely demonstrating a renal venous-arteriolar reflex. The pathway of the reflex courses outside of the kidney substance. A portion of the vasoconstriction observed, however, is dependent upon still undetermined local factors.

SUMMARY IN INTERLINGUA

Le sistema del vasos dextero-renal de pentobarbitalisate e laparotomisate canes
esueva testate relative al presenzia de un reflexo “venivasomotori” o “venose-arteriolar.” Elevation del renal pression venose e arterial, con flusso constante, esueva associate con un significative augmento immediate del resistentia vascular in le ren innervate. Le mesme manovra non resultava in le produzion de significative alterationes del resistantia in renes disnervate o disnervate e tractate con injectiones de agentes sympatholytic. Elevation del pression arterial sed non del pression venose esueva associate con alterationes del resistantia que non differeva significative-mente in renes innervate e in renes disnervate. Iste constatationes es interpretate como un demonstration probabil del existentia de un renal reflexo venose-arteriolar. Le via de iste reflexo es foras del substantia renal. Xonobstante, un parte del vasoconstriction observate depende de factores local que es non aurora determinate.

REFERENCES

A Hygrometer for Quick Determination of Specific Gravity of Body Fluids

From the specific gravity of whole blood and serum it is possible to calculate total serum protein, hemoglobin concentration and oxygen capacity. A quick method for determining specific gravity is, therefore, often useful for experimenters as well as clinicians.

A dilution hygrometer is described in which small quantities of blood, serum or other body fluid are placed and diluted with water until a tiny specific gravity ball, placed in a lower screened chamber, comes to rest. Specific gravity of the tested fluid is read directly on a graduated scale by the level of the diluted column.

Tests indicate that values for specific gravity so determined agree almost perfectly with those obtained by use of the copper sulfate method of Phillip and associates. There is no indication whether the N-N hygrometer is available commercially.

Effect of Elevation of Intraluminal Pressure on Renal Vascular Resistance
FRANCIS J. HADDY, Jerry Scott and Edwin Armstrong

Circ Res. 1956;4:659-663
doi: 10.1161/01.RES.4.6.659

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/4/6/659

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/