EFFECT OF EXPERIMENTAL NEUROGENIC HYPERTENSION ON
RENAL BLOOD FLOW AND GLOMERULAR FILTRATION RATES
IN INTACT DENERVATED KIDNEYS OF UNANESTHETIZED
RABBITS WITH ADRENAL GLANDS DEMEDULLATED

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This study was undertaken to examine responses made by the renal circulation to increases in systemic blood pressure in unanesthetized animals. The kidneys were denervated and the adrenal glands demedullated to avoid such nervous or hormonal effects as might be reflexly induced by the procedure employed in neurogenically obtaining pressure increases via severing the depressor nerves and clamping the carotid arteries. Interest in this problem stems not only from the general importance of an understanding of basic pressure-flow relationships, but also from the attention directed to alterations in renal blood flow as an explanation of the possible role of the kidney in the genesis of hypertensive disease.

It has been repeatedly shown that the most characteristic feature of the renal circulation is the constancy of renal blood flow which is maintained despite extensive variations in blood pressure. This was demonstrated in a classic experiment by Burton-Opitz and Lucas in 1911 (1). Renal blood flow was measured by stromuhr on the renal vein in dogs narcotized with chloroform or ether, and rises in arterial blood pressure were obtained by central excitation of the vagi. Characteristically no change in blood flow was detected despite pronounced rises in arterial blood pressure. This led them to conclude that the renal blood vessels tonically retain the normal size of the bloodbed. After renal denervation, in this preparation, the accommodation in increased pressure was lost and the renal blood flow was readily altered passively. However, Opitz and Smyth showed in dogs narcotized with morphine-pernactone that blood pressure variations elicited by the carotid sinus reflex did not alter renal blood flow as measured by stromuhr in intact or in denervated kidneys (2). The early literature dealing with the effect of changing pressure on renal blood flow as estimated by oncometer and stromuhr in anesthetized animals has been reviewed by Smith (3).

An opportunity to measure renal blood flow and glomerular filtration rates in unanesthetized animals was provided with the introduction of clearance techniques. Bing, Thomas and Waples (4) induced chronic hypertension neurogenically in dogs, and demonstrated that the renal blood flow and glomerular filtration rates remained constant or fell with the onset of increased blood pressures. The studies on the unanesthetized rabbit reported in this paper indicate

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2 Died August 7, 1940.
that this adjustment to acute pressure increases is made without the mediation of reflex nerve action or secretory activity of the adrenal medulla.

METHODS. Renal clearance procedures employed in this study were discussed in detail in an earlier paper (5). Renal plasma flow was measured as the p-aminohippurate clearance. The glomerular filtration rate was represented by the creatinine clearance, and estimation of the number of functioning glomeruli was obtained by calculation of the amount of glucose reabsorbed by the renal tubules when the glucose plasma level was high enough to ensure saturation of those tubules being perfused by glomerular filtrate.

The male rabbits used in this study varied in weight between 2.2 and 3.8 kgm. At least 3 weeks before the acute experiment the kidneys were denervated by completely stripping the renal pedicles and the adrenal glands were demedullated.

Blood pressure was measured directly by cannulation of the femoral artery. Under local anesthesia the depressor nerves were severed and, following several control periods, elevated systemic blood pressure was induced by clamping the carotid arteries. Blood and urine samples were collected before and after elevation of blood pressure and chemical analyses were made for creatinine, glucose, and p-aminohippurate in each. Blood hematocrits were recorded and specific gravity of blood samples determined by the copper sulfate solution method.

Measurement of retraction of the nictitating membrane of the eye was used on 3 animals to test the possibility that detectable amounts of adrenaline were liberated by the experimental procedure used to raise blood pressure. To test the possibility that denervation was not complete and that renal response to the neurogenic hypertensive procedure might be reflex, the vagus nerve was stimulated electrically to keep the blood pressure normal while the carotid arteries were clamped in 3 animals with adrenals demedullated and kidneys denervated.

RESULTS. The effects of increased blood pressure, neurogenically induced, were measured on the kidneys of 10 male rabbits which previously had their kidneys denervated and adrenal glands demedullated. Figure 1 illustrates an experiment in which, after 3 control periods of 21, 26, and 15 minutes each, the mean systemic blood pressure was raised from 75 to 110 mm. Hg by clamping the carotid arteries following section of the depressor nerves. This elevated pressure was maintained for 9 minutes. During the last 17 minute period the carotid circulation was restored by removing the clamps. The 47 per cent increase in pressure resulting from clamping the carotids did not significantly alter renal plasma flow (p-aminohippurate clearance), or glomerular filtration rate (creatinine clearance). In the period before clamping the carotid arteries the renal plasma flow was 72 ml. per minute and the glomerular filtration rate was 23.9. After the blood pressure was raised these values were 73 and 24.8 ml. per minute respectively. The number of functioning glomeruli (glucose Tm) was actually diminished with the elevation in pressure. Forty-seven and nine-tenths milligrams per minute of glucose were reabsorbed by the tubules in the period with the pressure at 75 mm. Hg, and 45.9 mgm. per minute at the elevated pressure.
Figure 2 represents the effect of elevated blood pressure on renal plasma flow in all the animals studied. The mean control systemic pressure in the femoral artery was 79 mm. Hg, and the mean increase following clamping the carotid arteries was 34 mm. Hg. Renal plasma flow increased slightly in 6 experiments and actually decreased in 3. A mean pressure increase of 43 per cent resulted in such accommodation by these denervated kidneys that the mean plasma flow increase was only 5 per cent.

Fig. 1. Renal response to the elevation of systemic blood pressure in a large male rabbit (R64, 3.8 kgm.) whose kidneys were denervated and adrenal glands demedullated 3 weeks before the acute experiment. After 3 control periods during which the mean pressure, with depressor nerves cut, was 77, 76 and 75 mm. Hg respectively, the pressure was suddenly elevated to 110 mm. Hg by clamping the carotid arteries. This 47 per cent increase in pressure did not significantly affect the renal plasma flow (p-aminohippurate clearance), the glomerular filtration rate (creatinine clearance) or the filtration fraction. The elevation in urine flow is characteristic and was noted even in those experiments where an actual diminution in renal plasma flow and glomerular filtration rate was induced with increased blood pressure. Renal plasma flow, glomerular filtration rate and urine flow are expressed as ml./min.

The effect of increased systemic blood pressure on glomerular filtration rate is illustrated in figure 3. A rise in filtration rate accompanied the increase in pressure in every experiment but one, but, as with renal plasma flow, the slight increase in rate indicated that an adjustment to pressure rise was made in these denervated kidneys which prevented the filtration rate from passively following the pressure increase. The 43 per cent mean systemic pressure increase resulted in raising the mean glomerular filtration rate only 8 per cent. The number of functioning glomeruli paralleled, in general, the glomerular filtration rate.
When Lamport's formulas were used to calculate renal afferent and efferent arteriolar resistance (6) it became apparent that the adjustment made by the kidney to pressure rises was chiefly an increase in resistance, presumably vasoconstriction, afferent to the glomeruli. Figure 4 illustrates the invariable increase in afferent resistance which accompanied increased systolic pressure, whereas no such uniform change in efferent resistance was noted.

Experiments were designed which demonstrated that the adjustment made by the kidney to pressure changes were not due, first, to incomplete denervation of the kidneys and, secondly, to reflex secretion of adrenaline induced by the experimental procedure employed in elevating blood pressure. In 3 rabbits with adrenals demedullated and kidneys presumably denervated the carotids were clamped following section of the depressor nerves, but blood pressure was prevented from rising by electrical stimulation of the vagus nerve. This did not induce increases in renal afferent resistance in any of the animals. The possible liberation of adrenaline following neurogenic pressure increase was tested in 3 other animals with adrenal glands demedullated and kidneys denervated.
of the nictitating membrane of the eye was used to test for the release of adrenine into the circulatory system. In 2 animals no retraction accompanied the procedure and in one rabbit a slight retraction was recorded. This indicated that it was quite unlikely that in these animals with adrenals demedullated the increase in renal afferent resistance was due to adrenine reflexly liberated from an extra-adrenal source.

![Graph](https://example.com/graph.png)

Fig. 3. The effect of elevated blood pressure on glomerular filtration rates in all rabbits examined. In all experiments but one (R6) the glomerular filtration rate rose with increased pressure but the rates did not passively follow pressure rises. The mean pressure increase was 43 per cent whereas the glomerular filtration rate increased only 8 per cent. Animal 74 had one kidney. All kidneys were denervated and adrenal glands demedullated.

**Discussion**

The experiments just described illustrate the autonomy of the renal circulation in the unanesthetized animal, particularly with reference to increases in systemic blood pressure. This relative constancy of renal blood flow at normal or high blood pressures has repeatedly been demonstrated (3, 4, 7–9). The observations here on the rabbit further demonstrate, however, that accommodation to pressure increases is obtained in totally denervated kidneys and without the mediation of adrenaline secretion.

Winton (9), Lamport (10) and Selkurt (7) have pointed out that as a consequence of filtration at the glomerulus post-glomerular blood undergoes hemoconcentration and increased viscosity until it is subsequently diluted by tubular...
water reabsorption. Should the glomerular filtration rate vary with blood pressure, corresponding alterations in viscosity would result in buffering the renal circulation against pressure fluctuations with the result that constant renal blood flow would be maintained. This explanation cannot be applied to the experiments in this study because the glomerular filtration rate, as well as the renal plasma flow, remained relatively constant despite marked increases in pressure. No increase in blood viscosity could be obtained which would be great enough to counteract the increased pressure produced. The failure of the filtration rate

Fig. 4. The effect of increased blood pressure on resistance in the renal circulation afferent and efferent to the glomeruli as calculated by Lamport's formulas. These results are from all animals studied and relate to the same data presented in figures 2 and 3. The increase in afferent resistance is achieved in these denervated kidneys presumably without the mediation of adrenine.

passively to follow blood pressure rises indicates that the accommodation in the renal circulation which resulted in uniform flow was made afferent to the glomeruli. The basic mechanism by means of which the renal circulation accommodates to elevations in blood pressure under these circumstances remains obscure.

**SUMMARY**

The relative autonomy of the renal circulation in unanesthetized rabbits, particularly with reference to increases in blood pressure, persists even in animals with kidneys denervated and adrenal glands demedullated.
Acute neurogenic blood pressure elevations were experimentally induced and clearance techniques employed to measure the effect of pressure increases on renal plasma flow and glomerular filtration rates in 10 male rabbits. A mean pressure rise of 43 per cent for all animals studied was accompanied by an increase in renal plasma flow of 5 per cent, and in glomerular filtration rate of 8 per cent. Three of the animals showed decreased renal plasma flow with the increase in blood pressure, and a fall in glomerular filtration rate was noted in one.

A rise in resistance afferent to the glomeruli accompanies blood pressure elevation. The basic mechanism accountable for this pressure-flow accommodation remains obscure.

REFERENCES

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