Sympathetic Vasoconstrictor Activity to the Kidney in Carotid Occlusion Pressor Reflex* (33836)

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(Introduced by E. J. Van Liere)

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By means of the "thermostromuhr," Rein *et al.* (1, 2) observed that renal flow in the dog remained almost unchanged on carotid occlusion when systemic arterial pressure rose considerably. With the clearance method, Kenny and Neil found that renal flow was normally increased by carotid occlusion and occasionally unchanged (3). Using a Shipley-Wilson rotameter, McGiff and Aviado (4) observed that mean renal venous outflow was nearly unchanged on carotid occlusion. Rises in arterial pressure with constant flow result in an increased peripheral resistance. An increase in renal peripheral resistance on carotid occlusion suggests that sympathetic vasoconstrictor fibers supplying the kidney were excited. However, according to Rein (1), renal flow remained unchanged in this pressor reflex even after severance of the renal nerve. This fact, which led to the idea of renal autoregulation, indicates that the above results are inconclusive as to the behavior of the renal nerve in the carotid occlusion pressor reflex.

The hemodynamic determinants of arterial pressure are mainly systemic resistance and cardiac output. Since cardiac output does not change significantly on carotid occlusion (5–9) the marked rise in arterial pressure is for the most part due to an increase in systemic peripheral resistance. The increase is so large that sympathetic vasoconstrictor activity seems to occur diffusely. The purpose of our study was to determine whether the renal vascular bed, which is highly specialized for urine formation, is also involved in this neural reflex in the absence of renal autoregulation.

Methods. Mongrel dogs of either sex weighing 8–14 kg were anesthetized with 30 mg/kg of sodium pentobarbital injected intravenously. As a maintenance dose, 5–10% of the initial dose was added at approximately 1-hour intervals. Experiments were interrupted for 15 min after each addition of the anesthetic. After cannulation of the trachea and saphenous vein, the animal was placed on its right side and the left renal artery was exposed retroperitoneally through a paravertebral incision. A 2.5- or 3-mm Statham electromagnetic flow probe was placed around the artery. Care was taken not to damage the renal nerves running adjacently. A polyethylene tube was placed in either the brachial or femoral artery and connected to a strain gauge pressure transducer. Renal flow and arterial pressure were recorded simultaneously on a pen recorder. Pulsatile changes were smoothed out with RC circuits to observe mean flow and pressure.

To keep mean arterial pressure of the animal constant, the left femoral artery was cannulated and connected to a bottle containing about 500 ml of heparinized blood (Fig. 1). The pressure of the blood reservoir was set at the resting level of mean arterial pressure of the animal by sending air into another bottle of 20 liters which was connected to the reservoir (Fig. 1 A). The temperature of the blood was kept near 38° by warming the reservoir from the bottom and side. When arterial pressure tended to change, blood automatically was withdrawn from or sent to the blood reservoir to minimize the pressure change. This method of blood pressure clamping was first used by Bayliss (10) in 1908 and thereafter improved by Krayer and Ver-

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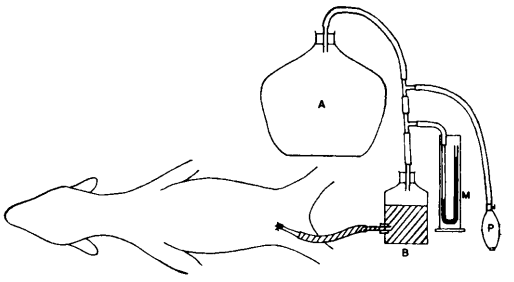

FIG. 1. The setup for blood pressure clamp, method of keeping mean arterial pressure constant by connecting the arterial system to a pressurized blood reservoir: (B), blood reservoir (500 ml); (A), air chamber (20 liters); (M), manometer; and (P), hand air pump.

ney (11) and Engelking and Willig (12). The animal was isolated from the pressure clamping system by applying a hemostat at the tube between the femoral artery and the reservoir.

For the nerve recording, one of the renal nerves was searched for between the left renal artery and vein and cut distally. The nerve was then desheathed and mounted on a pair of silver–silver chloride electrodes. The potentials were amplified by a RC coupled amplifier with an overall time constant of 0.02 sec, displayed on a cathode ray oscilloscope and photographed.

For both blood flow and action potential studies, the animal was kept on its right side. Vagi were intact and the animal was breathing spontaneously. The common carotid arteries were isolated bilaterally from the surrounding tissues in the neck for a length of about 5 cm so that they could be occluded with serrifines.

Results. Renal flow studies. When arterial pressure rose on bilateral occlusion of the common carotid arteries, renal flow remained almost unchanged or increased slightly (Fig. 2 A) before and after severing the renal nerves, confirming the previous observations by Rein (1). In a denervated kidney this constancy of flow against changes in head pressure is usually attributed to renal autoregulation. In an innervated kidney the same mechanism of autoregulation must be partly responsible for maintaining the flow unchanged during the carotid occlusion pressor reflex. The neural effects of carotid occlusion on renal flow in the innervated kidney were measured in 18 experiments with the blood pressure "clamped" (Fig. 2 B). The flow and pressure values were averaged, percentage changes were computed for the averaged values, and standard deviations of the percentage changes and preocclusion values were calculated. The results are summarized in Table I.

With the blood pressure clamp, the rise in blood pressure was slight on carotid occlusion. Renal flow diminished by 22.3 ± 9.3(SD)%. The t test revealed that this decrease was significant at $p = 0.005$. As shown in Fig. 2 B, in the earlier part of occlusion, arterial pressure rose transiently despite clamping. The readings of pressure and flow were done when this transient subsided and both pressure and flow became steady, usually more than 30 sec after the initiation of clamping. It was thought that the shift of blood into the reservoir from the animal had been completed by that time.

Renal nerve recordings. On carotid occlusion, activity in the renal nerve increased as in Fig. 3. Discharges became more continuous and the tendency to grouping with the pulse was obscured. Blood pressure rose gradually, following the increase in the nervous activity. The neurograms were recorded in a separate series of three dogs and a similar increase of nervous activity was observed in all of them. Since no vasodilators have been

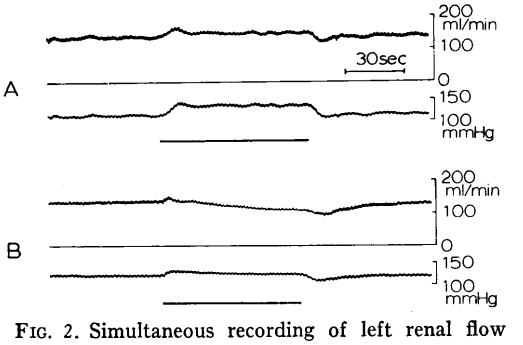

FIG. 2. Simultaneous recording of left renal flow (top) and arterial pressure (bottom): (A), without blood pressure clamp; (B), with blood pressure clamp. For the underlined period the common carotid arteries were occluded bilaterally.

TABLE I. Changes in Renal Flow and Arterial Pressure on Carotid Occlusion and Their Preocclusion Values.[a]

	Change (%)	Preocclusion value
Without blood pressure clamp		
Renal flow/body wt	2.5 ± 3.5	8.9 ± 2.7 ml/min/kg
Arterial pressure	26.5 ± 7.9	119 ± 9 mmHg
With blood pressure clamp		
Renal flow/body wt	−22.3 ± 9.3	8.9 ± 2.5 ml/min/kg
Arterial pressure	4.5 ± 2.0	120 ±11 mmHg

[a] Means of 18 expts. with SD.

proved in the renal nerve, all nervous activity was regarded as that of vasoconstrictors.

Discussion. When rises in arterial pressure were inhibited by the blood pressure clamp during carotid occlusion, renal flow was significantly diminished. This strongly suggests that sympathetic vasoconstrictors to the kidney were excited in the carotid occlusion pressor reflex. Catecholamine release from the adrenal medulla might be playing a part in increasing renal peripheral resistance. However, the effect of such blood-borne transmitters is believed to be minimal as compared to that of locally liberated ones at the nerve endings (13). An increase of nervous activity was observed in electroneurograms recorded in the renal nerve to confirm the above conclusion from flow recordings.

As previously reported (1, 2, 4), when the blood pressure is permitted to rise in the carotid occlusion pressor reflex, renal flow remains almost unchanged. This constancy of renal flow against the rise in arterial pressure is achieved by an increase in renal peripheral resistance. Vasoconstrictor fiber activation and autoregulation would be the two major mechanisms for this increase. Renal autoregulation refers to the phenomenon whereby changes in arterial pressure produce little or no change in renal blood flow in the denervated, perfused kidney. In the present study, it was shown that the increase in renal peripheral resistance occurred even after elimination of autoregulation by minimizing the blood pressure rise.

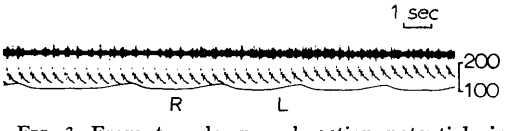

FIG. 3. From top downward, action potentials in the renal nerve, arterial pressure, and respiration (inspiration upward, recorded with a thermistor in the tracheal cannule): scale for pressure in mmHg. The right common carotid artery was occluded at R and the left one at L.

Summary. Renal flow was recorded by an electromagnetic flow meter in anesthetized dogs to observe the behavior of sympathetic nerve induced vasoconstriction to the kidney. Mean arterial pressure was held nearly constant by a blood pressure clamping procedure to eliminate autoregulation which would obscure the neural effect on renal resistance. Without the blood pressure clamp, renal flow remained almost unchanged when arterial pressure rose markedly on carotid occlusion. With the blood pressure clamp, renal flow decreased significantly on carotid occlusion. Renal electroneurograms showed an increased activity during carotid occlusion. Thus, sympathetic vasoconstrictor nerves to the kidney are excited in the carotid occlusion pressor reflex. It is concluded that the renal circulation participates in this neural reflex, by undergoing vasoconstriction in the absence of renal autoregulation.

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Cholinergic Blockade and Growth Hormone Responsiveness to Insulin Hypoglycemia* (33837)

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The observation of high concentrations of cholinergic and adrenergic neurons in the hypothalamus (1) raises the possibility that the neurotransmitters, acetylcholine and catecholamines may influence hypothalamic control of pituitary hormone secretion. Previous studies have indicated an adrenergic control mechanism for growth hormone secretion (2). The present study was performed to search for an antagonistic cholinergic control mechanism.

During the course of this investigation a possible pitfall in interpretation of paired data obtained from provocative tests of growth hormone secretion on consecutive days was uncovered. The initial experimental design for this project differed from previous growth hormone studies performed in our laboratory (2, 3) in that the control and experimental studies were carried out on consecutive days. The consistently lower growth hormone response on the second day might have led to a serious misinterpretation had not the order of performance of the control and experimental procedures been randomized.

Methods. Eight apparently healthy male medical students, 20–27 years old, were selected for this study. Two intravenous insulin tolerance tests were performed on consecutive days. Atropine was given during either the first or second test alternately to all subjects. The second test was repeated on each subject following an interval of 2–5 weeks.

The subjects were instructed to abstain from smoking and to take nothing by mouth except water after 10 p.m. the night before the study. Each subject reported to the experimental room at 7 a.m., was weighed, and then put to bed. A slow intravenous infusion of 0.85% NaCl was begun through a 20-gauge needle in an antecubital vein. The indwelling needle was used for withdrawal of blood samples as well as for injections of insulin and drugs. A sphygmomanometer was placed on the opposite arm and blood pressure and pulse rate were monitored every 15 min throughout the experiment.

After a 30-min base-line period, glucagon-free insulin (0.1 U/kg) was injected. Blood samples were taken every 15 min during the base-line period and for 90 min after the insulin had been given. In the cholinergic blockade experiments, 1 mg of atropine sul-

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