STUDIES ON EXPERIMENTAL HYPERTENSION

VI. The Effect of Section of Anterior Spinal Nerve Roots on Experimental Hypertension Due to Renal Ischemia*

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It has been shown that, in the dog, neither section of the renal nerves (1, 2) nor excision of the thoracic portion of the splanchnic nerves and lower four thoracic sympathetic ganglia (3) can prevent or reduce the type of hypertension which can be produced in animals (dog and monkey) by constricting the main renal arteries by means of a special clamp (4, 5). Recently it has been reported (6) that even total thoracic and abdominal sympathectomy, including cardiac denervation, does not prevent or lower hypertension in dogs produced by the same method.

This report deals with the effect of section of anterior spinal nerve roots from the sixth dorsal to the second lumbar inclusive in preventing or reducing the persistent hypertension which can be produced in normal dogs by constricting the main renal arteries.

EXPERIMENTS

In four dogs, by a single operation on each, under ether anesthesia, the anterior nerve roots of the spinal cord from the sixth dorsal to the second lumbar inclusive were severed. This was effected through a dorsal midline incision and laminectomy. The mean blood pressure of these animals was determined during the entire period of the experiment by a direct method. This consisted of the insertion into the femoral artery of a 21 gauge needle connected to a mercury manometer by rubber tubing filled with 2 per cent sodium citrate. Stopcocks were so arranged as to permit the building up of pressure in the manometer from a reservoir

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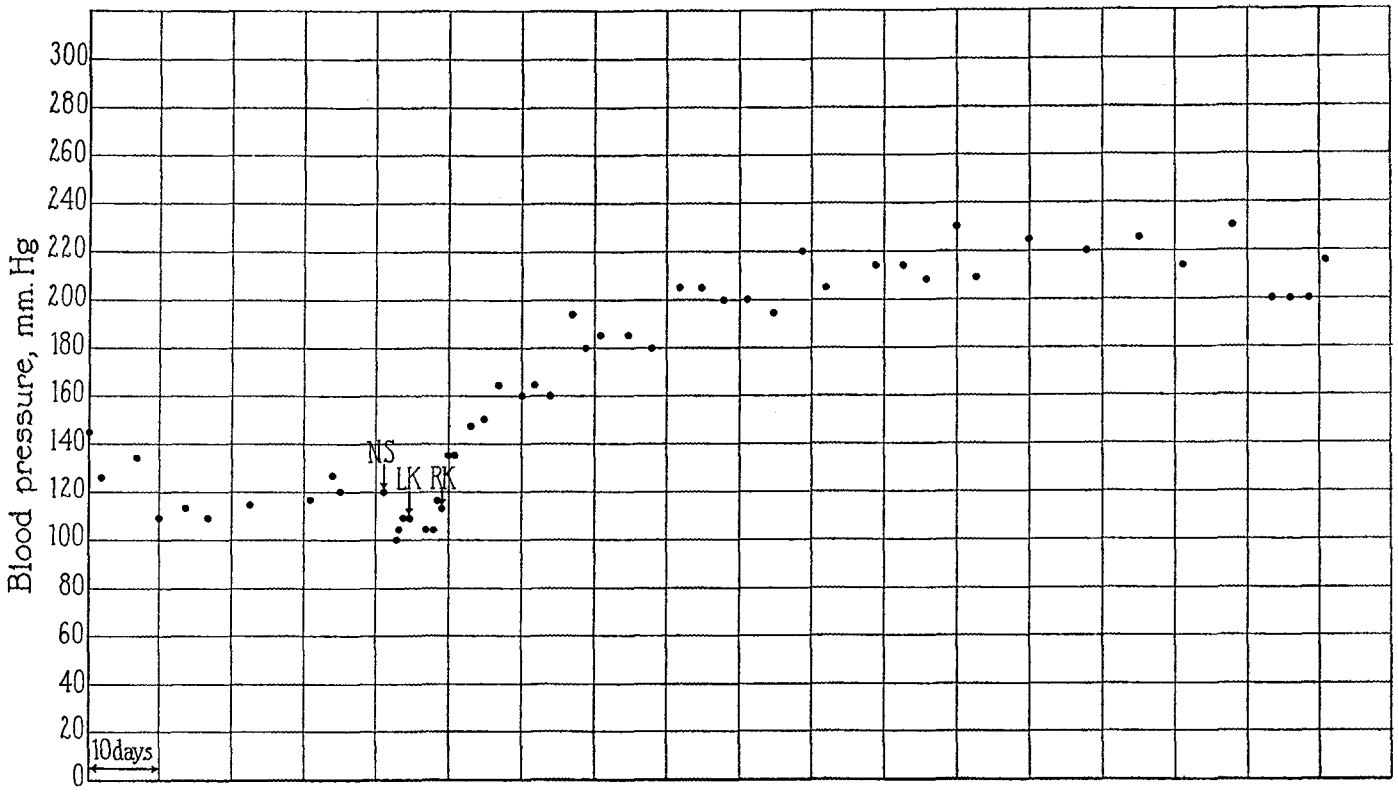
of sodium citrate and, after the insertion of the needle into the artery, the instantaneous communication of the manometer with the interior of the vessel. If the femoral nerve is avoided, the procedure appears to be quite painless and the animal remains very quiet during the determination. Only mean blood pressure is determined by this method but it has the advantage of being entirely objective. The length of the control period before the operation for section of the anterior nerve roots varied from 4 to 6 weeks. Another control period of from 4 days to 2 weeks was allowed between section of the anterior nerve roots and the application of the clamp for constriction of the first renal artery. A short interval was also permitted between the operations for constriction of both main renal arteries.

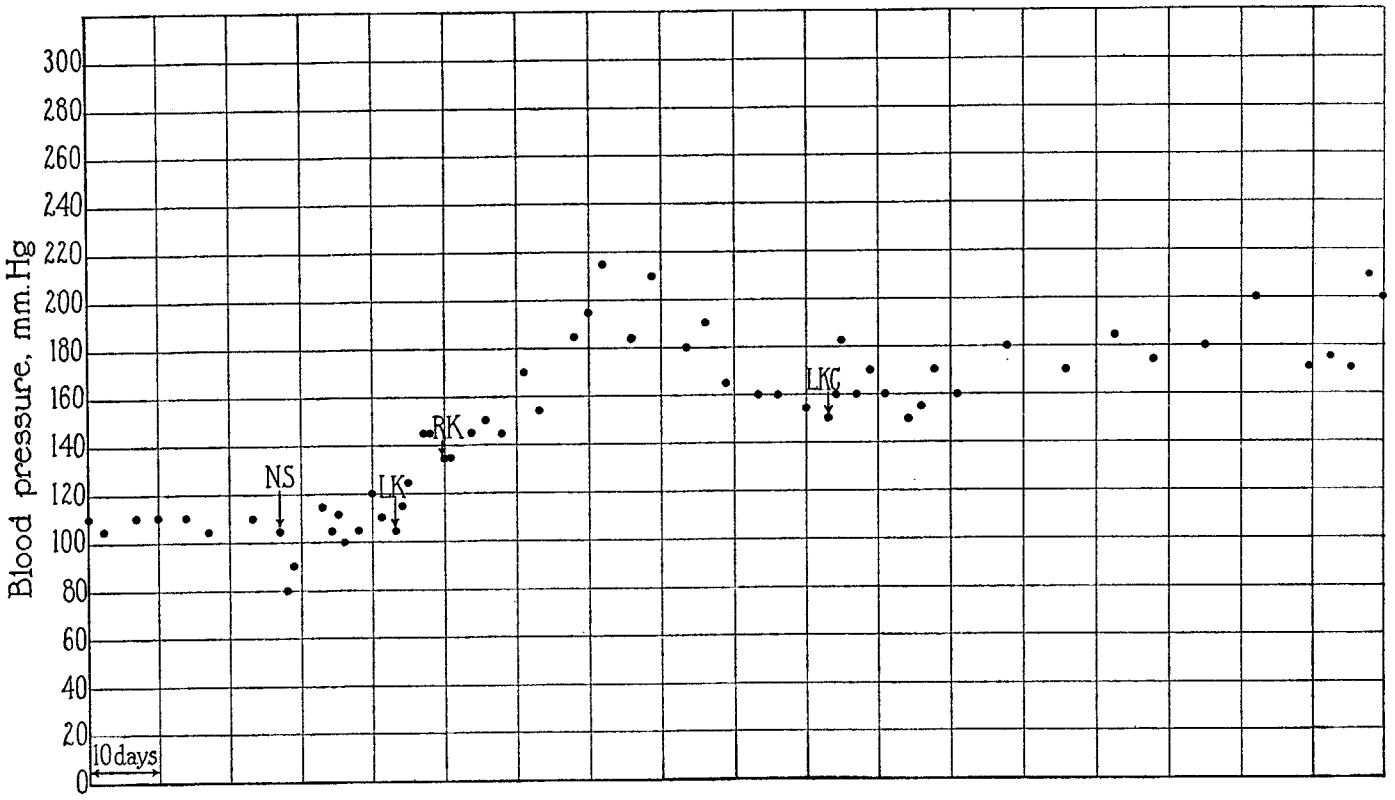
RESULTS

In all four dogs the mean blood pressures either remained unchanged or fell slightly below their normal level for a varying period after section of the anterior nerve roots. In one dog, No. 3-03, it was still slightly lower, but in others it was at the original normal level at the time of constriction of the first renal artery. After permanent constriction of one renal artery, the mean blood pressure became slightly to moderately elevated in three of the four dogs. In one dog, No. 3-09, (Text-fig. 1) it remained unchanged during the 4 days which intervened between the clamping of the left and right main renal arteries. After permanent constriction of both main renal arteries, the blood pressure of the four dogs rose to a higher level and this elevation persisted or even increased. This is well shown in Text-figs. 1 and 2, which illustrate the mean blood pressure of dogs 3-09 and 3-10, respectively, throughout the entire experimental period. Dog 2-75 showed moderate elevation of mean blood pressure following the constriction of one main renal artery but it died before the clamping of the other artery was attempted. Dog 3-03 also developed elevated blood pressure, but after about 4 weeks it tended toward a lower level without actually returning to normal. This occurs occasionally in dogs with the renal arteries constricted and is probably due to the effect of the accessory circulation which may become very great and necessitates increased constriction of one or both renal arteries to re-elevate the pressure. In dog 3-03 the clamp on the left renal artery (the first one constricted) was tightened 3 months after it was applied. This resulted in re-elevation of the mean blood pressure which is now, 2 months later, usually from 65 to 75 mm. higher than it was before the application of the first clamp. All but dog 2-75 are still alive.



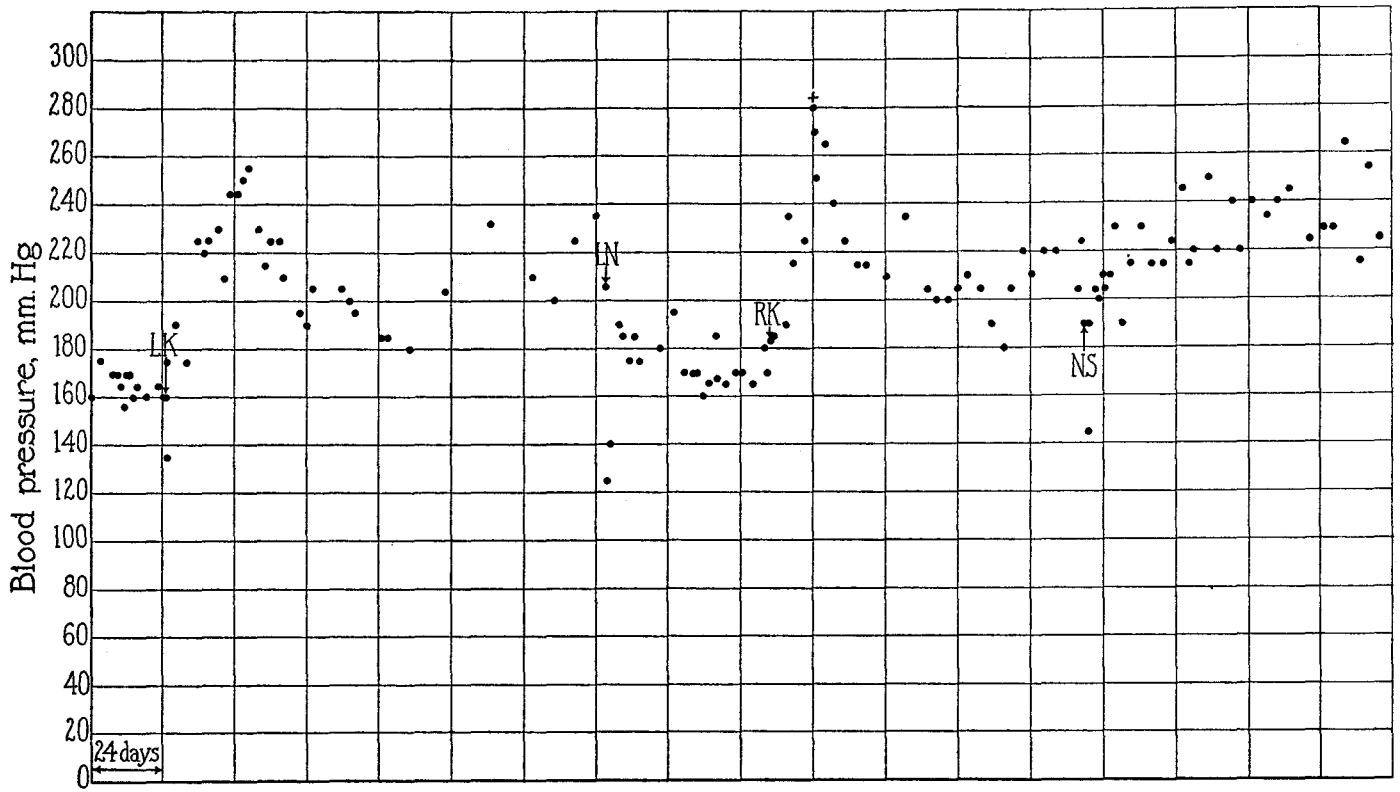
TEXT-FIG. 1. Dog 3-09. Female mongrel bulldog. Weight 10.2 kilos. NS, section of anterior spinal nerve roots from sixth dorsal to second lumbar inclusive. LK, constriction of left main renal artery. RK, constriction of right main renal artery.

The mean blood pressure became elevated after constriction of both main renal arteries.



TEXT-FIG. 2. Dog 3-10. Female mongrel bulldog. Weight 10.6 kilos. NS, section of anterior spinal nerve roots from sixth dorsal to second lumbar inclusive. LK, moderate constriction left main renal artery. RK, moderate constriction right main renal artery. LKC, complete constriction left main renal artery.

The mean blood pressure became elevated after the constriction of both main renal arteries.



TEXT-FIG. 3. Dog 2-68. Female mongrel bulldog. Weight 15.2 kilos. LK, moderate constriction left main renal artery. LN, left nephrectomy. RK, moderate constriction right main renal artery. NS, section of anterior spinal nerve roots from sixth dorsal to second lumbar inclusive. +, more than 300 mm. Hg, mean blood pressure.

The mean blood pressure remained elevated after section of the anterior spinal nerve roots (NS).

In two dogs, Nos. 2-68 and 2-35, hypertension was first produced and the anterior nerve roots were sectioned after the blood pressure had remained elevated for several months. In dog 2-68 (Text-fig. 3), the left main renal artery was first constricted. This was followed by the development of moderate hypertension which persisted, with a tendency downward, for about 5 months. As part of another study (7), the ischemic left kidney was then excised. This was followed promptly by a return of the mean blood pressure to the normal level and it remained at that level for 2 months. The main artery of the remaining right kidney was then constricted. The mean blood pressure rose to a very high level for a short time and then persisted at a lower but greatly elevated level. After 15 weeks of persistent hypertension, the anterior nerve roots from the sixth dorsal to the second lumbar inclusive were severed. The blood pressure has remained elevated after this procedure and has shown a gradual tendency upward (Text-fig. 3). The dog is still living. In the other dog, No. 2-35, systolic blood pressure was determined regularly throughout the entire experimental period by the van Leersum carotid loop method and occasionally by the direct method. The mean systolic pressure during a control period of 10 weeks was 158 mm. Hg. In this dog, bilateral splanchnic section within the thorax and excision of the lower four thoracic sympathetic ganglia failed to prevent the development of hypertension due to constriction of both main renal arteries (3). During the period between section of the splanchnic nerves and constriction of the first renal artery, the mean systolic pressure was 163 mm. Hg. After constriction of both main renal arteries, the mean systolic pressure was 244 mm. Hg. After this moderate degree of hypertension had persisted for more than 13 months, the anterior nerve roots from the tenth dorsal to the second lumbar inclusive were severed. There was a prompt fall of systolic and mean blood pressure after the operation and they remained lower for several weeks but did not fall to the normal level for this dog. Gradually the blood pressure has increased and now, 3 months after section of the anterior nerve roots, it is almost back to the high level at which it was before the section of the anterior nerve roots. During the last 2 weeks the systolic pressure has varied between 220 and 240 mm. Hg.

DISCUSSION

The failure of section of the anterior spinal nerve roots, from the sixth dorsal to the second lumbar inclusive, to prevent or reduce hypertension which can be produced by constriction of the main renal arteries (4, 5) is interpreted as due to the persistence of the effect of such constriction as long as the clamps remain applied. The same explanation applies to the failure of the other surgical procedures that have been carried out on the nervous system of dogs (1, 2, 3, 6) to affect this type of experimental hypertension, for none of these procedures has any effect on the clamp. These experiments make it very unlikely that the origin of this type of hypertension is due to a reflex from the ischemic kidney. They also minimize the part played by the nervous portion of the vasomotor apparatus of all parts of the body except the kidney in initiating the elevation of the blood pressure. Persistent or frequent stimulation of the vasoconstrictor nerves of the kidneys alone would probably produce hypertension by constricting the arterioles and reducing the blood supply to the functioning components of the kidney. The rest of the mechanism would be the same as that following constriction of the main renal arteries. This is being investigated at the present time. The probability is great that the mechanism whereby constriction of the main renal arteries results in hypertension is a humoral one, with a hypothetical effective substance of renal origin producing direct constriction of the muscle of the arterioles. This has been discussed at greater length in another publication (7). Since it is the narrowing of the arterioles and not of the main renal arteries that is associated with vascular hypertension in man, it is at least possible that section of vasoconstrictor nerves to the kidneys of hypertensive individuals would result in relaxation of the wall of renal arterioles in which the organic changes are not fixed. Improvement of the blood supply to the functioning components of the kidneys would occur. Lowering of blood pressure has been reported in about the same percentage of cases as a result of a number of different surgical procedures on the nervous system (8–17). Common to all is section of the vasoconstrictor nerves to the kidneys. This indicates that in all cases the beneficial effect may be due to

the relaxation of renal arterioles and improvement of circulation to the functioning components of the kidneys and not, as has been suggested, to the relaxation of arterioles in a large part of the vascular bed in the abdomen. The failure of these same procedures to affect experimental hypertension due to constriction of main renal arteries does not in any way controvert the results obtained in human hypertension. It merely emphasizes the importance of reduced blood supply to the kidneys in the pathogenesis of this type of experimental hypertension and perhaps in human hypertension that is associated with renal arteriolar sclerosis.

SUMMARY

Section of the anterior spinal nerve roots from the sixth thoracic to the second lumbar inclusive did not prevent or significantly and permanently reduce hypertension produced by constricting the main renal arteries of dogs. The significance of these results for the pathogenesis of human and experimental hypertension is discussed.

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