11407 P

Rôle of the Sympathetic Nervous System in Experimental Neurogenic Hypertension.

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Recent clinical studies[1] have renewed interest in central or psychosomatic factors in essential hypertension. The sustained neurogenic hypertension in dogs described by Heymans and Bouckaert[2] seems from this point of view to afford a better experimental approach to the problem of hypertension and sympathectomy than the renal hypertension described by Goldblatt,[3] and shown to be uninfluenced by total sympathectomy.[4–7] The recent demonstration, Grimson, Bouckaert and Heymans,[8] that a sustained neurogenic hypertension of renal origin may be produced by a central reflex mechanism tends to correlate these two methods for producing experimental hypertension. The present study is based upon an effort to determine the blood pressure levels produced by section of the depressor nerves in normal dogs and compare them with the pressure levels produced by the same procedure in dogs sympathectomized with the exception of the nerve supply to the kidneys and adrenals, as well as to study the effects of renal denervation, splanchnic resection, and total paravertebral sympathectomy on the former group.

Heymans and Bouckaert[9] have shown that section of the depressor nerves produces a persistent hypertension and that total sympathectomy eliminates the hypertension. Goldblatt, Kahn, Bayless and Simon[10] have recently failed to obtain this type of hypertension

1 Katz, L. N., and Leiter, Louis, *Psychosomatic Med.*, 1931, **1**, 101.

2 Heymans, C., and Bouckaert, J. J., *C. R. Soc. Biol.*, 1931, **106**, 471; *Bull. Acad. Roy. Med. de Belg.*, 1939, p. 441.

3 Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W., *J. Exp. Med.*, 1934, **59**, 347.

4 Alpert, L. F., Alving, A. S., and Grimson, K. S., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 1.

5 Freeman, N. F., and Page, I. H., *Am. Heart J.*, 1937, **14**, 405.

6 Heymans, C., Bouckaert, J. J., Bayless, F., and Samaan, A., *C. R. Soc. Biol.*, 1937, **126**, 434.

7 Verney, E. B., and Vogt, M., *Quart. J. Exp. Physiol.*, 1938, **28**, 253.

8 Grimson, K. S., Bouckaert, J. J., and Heymans, C., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 225.

9 Heymans, C., and Bouckaert, J. J., *C. R. Soc. Biol.*, 1935, **120**, 82.

10 Goldblatt, H., Kahn, J. R., Bayless, F., and Simon, M. A., *J. Exp. Med.*, 1940, **71**, 175.

and Nowak and Walker[11] have stated that some hypertension follows depressor nerve section in sympathectomized dogs. These contraindications have further stimulated this study.

In 9 dogs both carotid sinuses were excised, the left vago-sympathetic-depressor nerve was cut, and a segment of the right sympathetic depressor trunk was removed. The control blood pressures were respectively 131, 133, 134, 134, 138, 138, 144, 148 and 174. These dogs were observed from 16 to 163 days after modulator nerve section and their pressure readings averaged respectively 238, 246, 239, 212, 194, 256, 257, 214 and 226. The late readings in 3 animals were appreciably higher than the early readings. Three animals had occasional readings of 280 to 300. None of the dogs failed to develop a hypertension and in none of them was there any late lowering of the hypertension.

In 6 normal dogs both paravertebral sympathetic chains were removed. Their control blood pressures averaged 142 and their pressures 14 to 29 days after sympathectomy averaged 112. Because of the observation (Grimson, Wilson and Phemister[12]) that sympathectomized dogs recover in a few months a new central vasomotor mechanism and restore their preoperative blood pressure the modulator nerves in these dogs were sectioned in the manner described above 14 to 29 days after the sympathectomy. Two dogs died shortly after operation without pressure elevation. The other 4 during the next 30 days had an average pressure of 98. No elevation was observed. Two were observed 90 and 108 days and developed pressures higher than before the sympathectomy, 164-206. Two other dogs sympathectomized 26 and 28 months previously and with restoration of their blood pressure to averages of 148 and 152 developed average pressures after modulator nerve section of 169 and 176 mm respectively with occasional readings of 200. This observation of levels higher than before sympathectomy suggests that the recovered central vasoconstrictor mechanism[12] is influenced by the modulator nerves.

Seven dogs* have now been sympathectomized with the exception of the splanchnic supply to the adrenals and kidneys according to the described technic.[8] Their blood pressures just preceding modulator nerve section averaged 136 and during several weeks afterward 195. This elevation is definitely less than the average of the nine normal dogs with modulator nerve section described above which

[11] Nowak, S. J. G., and Walker, I. J., *New England J. Med.*, 1939, **220**, 269.

[12] Grimson, K. S., Wilson, H., and Phemister, D. B., *Ann. Surg.*, 1937, **106**, 801.

* Three observed in Prof. C. Heyman's laboratory in Ghent.

was 231. Renal denervation in four of these 7 dogs has restored their pressure to about the normal level.

Further experiments have shown that renal denervation alone neither prevents nor appreciably alters the hypertension produced in normal dogs by modulator nerve section. They have also confirmed the observations of Nowak and Walker[11] that abdominal sympathectomy and division of the splanchnic nerves as well as complete sympathectomy except for one thoracic chain fails to restore the blood pressure of neurogenic hypertensive dogs to normal. Total sympathectomy as described above lowered the pressure of 3 neurogenic hypertension dogs from 239, 226 and 246 to 101, 122 and 91 respectively during 30, 18, and 40 days of observation. After 30 and 40 days in 2 of these animals blood pressure recovery was evident and progressed toward a moderate hypertension level. This parallels but exceeds the recovery following paravertebral sympathectomy in normal dogs previously reported.[12]

11408 P

Renal Phosphatase in Experimental Nephropathies.*

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The specific function of the rich phosphatase content of the kidney is still unknown. Since the kidney is almost invariably involved in metastatic calcification and is often the site of pathologic calcification it seemed possible that by comparing the location of the deposits of lime salts in these conditions with that of the phosphatase something might be learned concerning the relation of this enzyme to renal function.

For this purpose we studied phosphatase, acting optimally at a pH of about 9.0 on sodium glycerophosphate, in the kidneys of normal dogs and of dogs in which a toxic nephrosis has been produced by uranium nitrate, potassium bichromate and bichloride of mercury. We compared sections stained for phosphatase by Gomori's[1] method with the quantity of the enzyme obtained in aqueous extracts of the cortical tissue of the same kidneys as determined by Bodansky's

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1 Gomori, G., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 23.