

LETTERS TO THE EDITOR

The Role of Adrenal Medulla in Maintenance of Cardiac Catecholamine Levels in the Rat

SIR.—It is known that tissues with postganglionic sympathetic innervation, including the heart, can take up noradrenaline from the blood or from the surrounding fluid (Raab and Gige, 1955; Axelrod, Weil Malherbe and Tomchick, 1959; Bhagat, 1963; Bhagat and Shideman, 1963b,c). This indicates that catecholamines discharged into the blood stream from the adrenal gland and sympathetic nerve endings could supply the heart. Bhagat and Shideman (1963a) have shown that the heart is probably capable of synthesizing noradrenaline from its precursors dopa and dopamine in intact animals. We now describe work undertaken to obtain information on the role of the adrenal medulla in the maintenance of the neurotransmitter store in the intact animal. 1-(5,6-Dimethoxy-2-methyl-3-indole)-ethyl-4-phenylpiperazine (Win 18501-2, Oxyperitine) was employed as a pharmacological tool for depleting the heart of its catecholamine stores and the influence of a reduced supply of circulating catecholamines, as produced by adrenal demedullation, on repletion of these stores was determined.

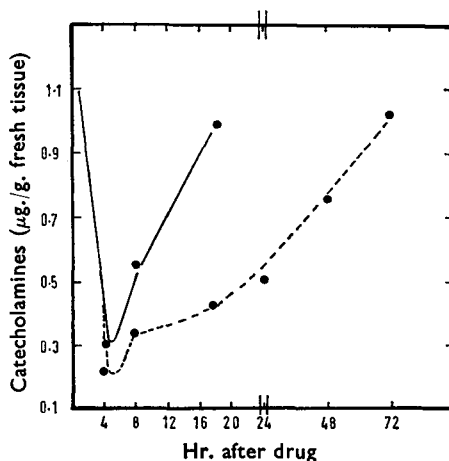


FIG. 1. Effect of adrenal demedullation on the repletion of cardiac catecholamines. Solid lines indicate normal animals. Broken lines indicate demedullated animals. Each amine level is mean of 5 or 6 values.

Male rats (Holtzman strain) weighing 200 to 225 g. were either demedullated or sham operated as described by Bhagat and Shideman (1963a). Ninety-six hr. after the operation, the rats were given Win 18501-2, 50 mg./kg. intraperitoneally, and killed at various times thereafter. The concentrations of catecholamines in the ventricular myocardium were determined by the trihydroxyindole fluorimetric procedure of Shore and Olin (1958) and expressed as $\mu\text{g.}$ of noradrenaline per g. of fresh tissue.

The results (Fig. 1) show that noradrenaline returned to control value in the sham operated rats within 18 hr. after Win 18501-2. This suggests that turnover of noradrenaline in the heart is rapid. While demedullation retarded significantly the restoration of cardiac catecholamine in the rats after Win 18501-2 treatment, thereby showing the importance of an extra cardiac source in the maintenance of the neurotransmitter store, it had no effect on normal levels of catecholamines in the heart. There was no significant difference in myocardial

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catecholamine levels between sham operated and demedullated animals. These data indicate that the maintenance of normal levels of myocardial catecholamines is not totally dependent upon deposition of circulating catecholamines of adrenal origin or upon the presence of a functioning adrenal gland. This supports the view that the body has the ability to adjust itself to environmental conditions and this might be considered as a kind of compensation mechanism in the organism. When, for example, uptake of noradrenaline from the circulating blood was reduced by demedullation of the suprarenals, the heart, in order to maintain normal levels, probably increased the rate of synthesis of noradrenaline. Similarly, nervous excitation increases the rate of synthesis of catecholamines, for prolonged stimulation does not alter the noradrenaline content of nerves (Luco and Goni, 1948) or of ganglia (Vogt, 1956). Also, prolonged splanchnic stimulation brings about the release of catecholamines from the adrenal medulla but the concentration in the medulla decreases little (Elliott, 1912; Hökfelt and McLean, 1950; Holland and Schümann, 1956). On the other hand, infusion of both adrenaline and noradrenaline, at rates which may be considered to be physiological, inhibits the adrenal medullary secretion of catecholamines (Robinson and Watts, 1962).

Thus, the present study demonstrates that the turnover of heart noradrenaline in the rat is rapid and that uptake of catecholamine from the circulating blood is an important factor in maintaining the normal levels of catecholamines in the heart, though the heart is not totally dependent on extraction of noradrenaline from the blood.

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