LETTERS TO THE EDITORS

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Output of Sympathin from the Spleen

QUALITATIVE studies of the nature of 'sympathin', the vasopressor substance appearing in the venous blood after stimulating post-ganglionic adrenergic nerves, have shown that it consists of a mixture of adrenaline and noradrenaline. We have recently been investigating quantitative aspects of sympathin output from the spleen with particular attention to the effect of the frequency of stimulation.

The method used was to stimulate the splenic nerves of the chloralosed cat and to measure the sympathin, assayed as noradrenaline, appearing in the venous blood. Peart¹ and Mann and West² have shown that sympathin from the spleen is almost entirely noradrenaline. The spleen was isolated from the stomach, pancreas and omentum, but retained its own circulation. The venous blood from the organ could be temporarily diverted to a polythene cannula in the superior mesenteric vein by occluding the portal vein. The blood from the cannula was collected in chilled, silicone-coated centrifuge tubes containing solid heparin. These precautions prevented the formation of masking substances. The volume of the separated plasma was measured and its 'sympathin' content assayed on the pithed rat's B.P. The splenic nerves were stimulated with rectangular pulses known to be supramaximal. Since we were interested in the effect of the frequency of stimulation on the output, the total number of stimuli was kept constant at 200 stimuli irrespective of the frequency. Both adrenal glands were removed and both major splanchnic nerves cut.

The output of sympathin, expressed as output/stimulus, showed a remarkable variation with the frequency of stimulation. This is summarized in

Fig. 1. Mean output/stimulus of 'sympathin' plotted against the frequency of stimulation. At all frequencies of stimulation the total number of pulses was 200. The vertical lines represent the standard errors of the means. Figures for 100, 200 and 300 pulses per sec. are single observations

Fig. 2. First part of the graph in Fig. 1 with an extended scale for frequency. The individual results from three animals previously given 'Dibenamine' are shown. The output/stimulus at 10 pulses per sec. has increased and equals the maximum in the untreated animal. There is no obvious variation with frequency

Fig. 1. At low frequencies, little sympathin appears in the venous blood; but the output rises sharply as the frequency increases, to reach a maximum at about 30 pulses per sec. In constructing this graph allowance must be made for variations in the plasma flow in the period of collection. The output of sympathin varies with flow, and if this is reduced the output falls. The figures used in this graph lie in the same range of plasma flow.

Several explanations of this variation with frequency were possible. It might be that the more prolonged exposure to amine oxidase of the sympathin liberated at lower frequencies permitted a greater destruction of the active amine. This was tested by inhibiting the amine oxidase with isopropyl isonicotinyl hydrazine ('Marsilid'). The output before and after 'Marsilid' was the same.

Another possibility was that although the amount of sympathin released by each nerve volley was constant, the amount utilized by the tissue receptors was greater when the rate of release was slowed, that is, at low frequencies of stimulation. This was tested by blocking the tissue receptors with N.N. dibenzyl- β -chloroethylamine ('Dibenamine') and measuring the output/stimulus at varying frequencies. The results are shown in Fig. 2.

The first part of the previous graph has been drawn with an extended scale for frequency. Superimposed on it are the individual results for three experiments in which 'Dibenamine' had been given to the animal. The output at 10 pulses per sec. is increased some sevenfold and now equals the maximum output in the untreated animal. Furthermore the difference in output with frequency in this range has disappeared.

We suggest that the explanation of these observations is that the sympathin release per nerve volley is constant, and that the fraction utilized by the tissues is greater at the lower frequencies of stimulation.

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¹ Peart, W. S., *J. Physiol.*, **108**, 491 (1949).

² Mann, M., and West, G. B., *Brit. J. Pharmacol.*, **5**, 173 (1950).