Modified technique for recording perfusion rate

Electronic devices to record the perfusion pressure changes are expensive. A simple modification of the mechanical method of Sollman & Hanzlik (1939) has been made. Ringer solution from a reservoir flows from a height of 30–50 cm through pressure tubing to the animal. The reservoir has a Marriot's tube (inner diameter 3 mm) connected through pressure tubing to a deep large Mary's tambour with a diaphragm that is not taut. The only "air-inlet" is a hypodermic needle (no. 26) in the pressure tubing. A light straw recording lever magnifies diaphragm movements 15–20 times. Drugs are injected in volumes of not more than 0·5 ml, into the inflow tubing. The principle of the method is based on recording the degree of relative negative pressure created in the air inlet system using a sensitive tambour. The degree of relative vacuum depends on the rate of perfusion—the more the perfusion, greater the vacuum. The recording lever in the resting position (zero inflow) is at "zero" line. As the perfusion starts, the lever shifts downwards till it is stabilized to give a horizontal base line corresponding to the initial inflow rate. Responses of constrictor drugs are recorded by an upward shift and those of dilator drugs are recorded by a downward shift of recording lever from the control line.

The kymographic record can be calibrated either at the beginning or at the end of the experiment. Use of a screw clip on the perfusion tube allows the free flow of fluid to be varied in steps. At each such step, the rate of flow and the rate of bubbles from the Marriot's tube are recorded along with the shift of the lever on the drum. The number of bubbles from the Marriot's tube can thus be converted to its equivalent in volume of fluid. A graphic plot of the vertical shift from the zero outflow line, of the lever on the drum against the actual rate of inflow has been found to have a linear relation. Therefore, the calibration of the inflow records becomes easy. The calibration scale will always remain the same provided the tambour, its lever (degree of magnification), the air inlet needle and the reservoir with Marriot's tube remain unaltered.

The selection of appropriate size of "air inlet" needle is critical. In blood vessel perfusion experiments on small animals (frogs, albino rats, guinea-pigs, rabbits) a number 26 size hypodermic needle was sensitive enough to record a change of 1·0 ml/min flow by a 4 mm vertical shift of the lever on the drum. For larger animals (dogs, cats) a needle of larger bore is required. The vertical flicker of the lever due to the escape of individual bubbles provides a 1·0–1·5 mm width of the record. Records of the effects of varying doses of a vasoconstrictor and a vasodilator drug on the perfused blood vessels of frogs are shown in Fig. 1.

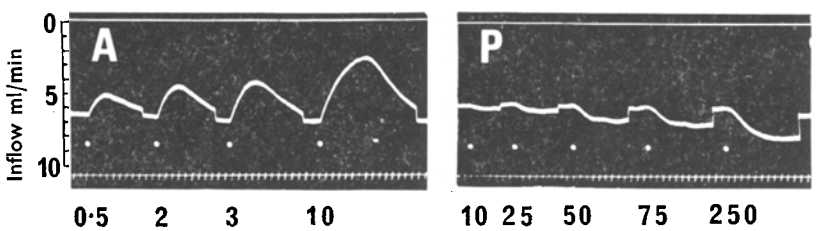

FIG. 1. Recordings of constrictor and dilator responses of perfused systemic blood vessels of a pithed frog. Each record shows from above downwards, the zero line, the perfusion pressure tracing and the time signals every 30 s. A. Constrictor responses of different doses of adrenaline (0·5, 2, 3 and 10 μg). P. Dilator responses of different doses of papaverine (10, 25, 50, 75 and 250 μg) on blood vessels, perfused with frog ringer containing barium chloride (100 μg/ml). A one and a half times increase in dose produces a notable increase in response.

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Effects of desipramine and cocaine on sympathetic responses in the pithed rat

Desipramine blocks the uptake of noradrenaline into sympathetic nerve endings (Hertting, Axelrod & Whitby, 1961; Iversen, 1965), and this has been accepted as the explanation for enhancement by desipramine of responses to adrenergic nerve stimulation and to exogenous noradrenaline. However, *in vitro* experiments with large doses of desipramine have demonstrated depression of sympathetic responses attributed to α-receptor blockade (Bonaccorsi & Hrdina, 1967; Bassett, Cairncross & others, 1969; Scriabine, 1969). Bonaccorsi & Hrdina (1967) reported that desipramine did not reduce responses to intravenous injections of noradrenaline in pithed rats. We now report the effects of desipramine and cocaine on the pressor responses to both intravenous injections of noradrenaline and sympathetic nerve stimulation in the pithed rat preparation described by Gillespie & Muir (1967). Desipramine was compared with cocaine since the latter drug does not have α-receptor blocking activity, but blocks uptake into sympathetic nerve endings (Muscholl, 1961).

The area of the pressor responses to sympathetic nerve stimulation and noradrenaline were measured by planimetry. The responses after desipramine or cocaine were calculated as a percentage of the mean control response. The results are illustrated in Fig. 1. Desipramine and cocaine in doses up to 2 mg/kg enhanced the pressor responses to sympathetic stimulation and intravenous noradrenaline. With higher doses the effects of the two drugs differed: cocaine continued to enhance the pressor responses whereas maximal enhancement was obtained with 2 mg/kg of desipramine and the enhancement was less with higher doses. The effect of both drugs on noradrenaline released from sympathetic nerve endings was far greater than the effects on injected noradrenaline. However, unlike Bonaccorsi & Hrdina (1967), some potentiation of injected noradrenaline by desipramine was demonstrated: the mean area of the pressor response to injected noradrenaline was 207 $\pm$ 47% of control with 2 mg/kg of desipramine. Unlike cocaine, the sharp cut off in the potentiating action of desipramine above 2 mg/kg can possibly be explained in terms of its dual action, namely: blockade of noradrenaline uptake demonstrated at low doses, and α-receptor blockade demonstrated at higher doses.

Desipramine antagonized calcium-induced contractions in a dose dependent manner (Bonaccorsi & Hrdina, 1967) so its blocking action in high doses could be due to a combination of α-receptor blockade and a membrane stabilizing effect.

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