**The limit of sensitivity of bioassay of catecholamines on the perfused arterial segment**

SIR,—The method of bioassay of catecholamines described by de la Lande & Harvey (1965) involved the injection of a solution of the catecholamine into Krebs bicarbonate solution with which a segment of the central artery of the ear of the rabbit was perfused. The volumes for injection must be small (0·4 ml or less) and approximately equal when comparisons are made between test and unknown solutions. These requirements can be avoided and a gain in sensitivity of some five fold achieved by perfusing the preparation with the solutions.

In each of six experiments, we have observed that the increase in perfusion pressure in response to an infusion of noradrenaline is sustained and is concentration dependent. The sensitivity is indicated by the average responses to noradrenaline, 0·5 ng/ml, in the above six experiments which were 5, 5, 10, 15, 19 and 20 mm of mercury respectively. The procedure does, however, raise a problem by requiring large volumes of test solution for infusion. This difficulty can be minimised by infusing, for brief periods only, i.e. 10–15 sec; this enables volumes of 1·0–1·5 ml to be tested. The response obtained is then not maximal but is reproducible and dose dependent (Fig. 1).

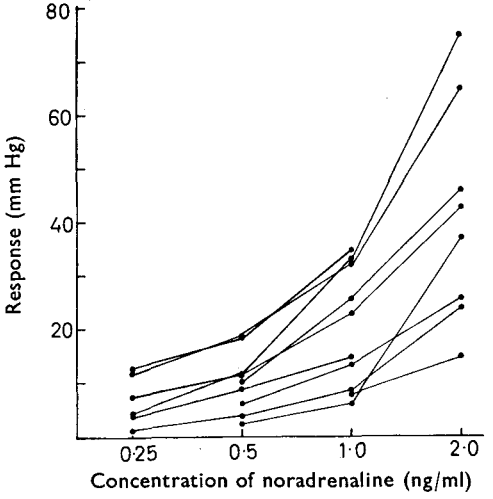


FIG. 1. The increases in perfusion pressure in response to 15 sec infusions of noradrenaline in ten arteries.

Brief infusions are given by stopping the perfusion pump during the short intervals (1–2 sec) required for the transfer of the outlet tubing between the reservoir of Krebs solution and the test solution (warmed at 37°) in a second reservoir. A dead space of 3–5 ml in the infusion system between reservoirs and preparation ensures that the record of the response to the catecholamine is unaffected by the preceding transient drops in pressure caused by brief interruptions to the perfusion.

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February 28, 1966

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## The effect of ascorbic acid on anaphylactic shock in dogs

SIR,—Many controversial reports about the effect of ascorbic acid on anaphylactic shock in different species are found in the literature. Recently, Dawson & West (1965a) showed that large doses, given just before the antigen challenge, protect guinea-pigs or rats from anaphylactic shock. In another paper, Dawson & West (1965b) reported that the protective action of ascorbic acid followed a direct effect on the bronchial muscle. The effect of ascorbic acid on anaphylactic shock in dogs has now been investigated.

Twenty-two dogs, 6·5 to 11·5 kg, were sensitized with horse serum (6 ml subcutaneously 5 times at 3-day intervals). About 22 days later, they were anaesthetised with intravenous chloralose (110 mg/kg) and injected intravenously with 20 ml of horse serum. Blood pressure recordings were made from the right carotid artery with a mercury manometer. Four of the dogs had no pre-treatment and served as controls. The sudden and excessive fall in blood pressure with congestion in the liver occurred immediately after the challenge with antigen in these four animals. Groups of 3 of the other 18 dogs were injected intravenously with ascorbic acid (500 mg/kg) either immediately or at 5, 10, 15, 20 or 30 min before the antigen challenge. This dose of ascorbic acid had no effect on anaphylactic shock, the blood pressure in all animals falling from about 110 to about 30 mm Hg, and most of them (85%) dying within 1 hr of challenge. Blood samples taken before and after anaphylactic shock were assayed for their histamine contents (Csaba, Szilagyi, Damjamovich & Kover, 1963), but no change was found in the amount of histamine liberated in anaphylaxis (controls increased about 50-fold whereas ascorbic acid-treated animals showed mean increases of about 41-fold).

Thus, ascorbic acid given before the antigen challenge in dogs has no protective action against anaphylactic shock and does not influence histamine release. The shock organ in dogs is the liver and not the lung as in guinea-pigs. The inability of ascorbic acid to influence the reaction in the dog thus adds weight to the hypothesis that ascorbic acid directly inhibits the bronchospasm in guinea-pigs and does not act solely through the adrenal system as some workers [for example, Guirgis (1965)] have suggested.

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March 2, 1966

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