SELECTIVE RELEASE OF CATECHOLAMINES IN EXPERIMENTAL CORONARY OCCLUSION

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Coronary occlusion is a potent stimulus for the release of catecholamines from the sympathoadrenal system. Richardson (1965) showed that coronary ligation in dogs produced a six-fold increase in the concentration of plasma noradrenaline during the first 24 to 36 hrs following occlusion. On the other hand, studies of the secretion of catecholamines during the initial phase of coronary occlusion (Staszewska-Barczak and Ceremuzynski, 1968) showed that adrenaline was the main, if not the only catecholamine, released into the circulation.

In most of the previous reports, the release of catecholamines following coronary occlusion were induced by ligation of the anterior descending branch of the left coronary artery in dogs (Richardson, 1965; Staszewska-Barczak and Ceremuzynski, 1968; Ceremuzynski, Staszewska-Barczak and Cedro, 1969; Staszewska-Barczak, 1971). The change in the concentration of catecholamines following occlusion of the right coronary artery has been given relatively less attention. This prompted us to compare the release of catecholamines following the occlusion of the anterior branch of the left coronary and the right coronary arteries in the same or different dogs.

METHODS

The experiments were done on dogs of both sexes weighing 10-25 Kg. Anaesthesia was induced and maintained with pentobarbitone. The lungs were mechanically ventilated; the heart was exposed through a middle sternostomy; ligatures were placed around the left anterior descending or right coronary arteries.

Circulating catecholamines were assayed continuously by the blood-bathed organ technique (Vane, 1969). Heparinised blood from the femoral artery of the dog was pumped at the rate of 10 ml/min to superfuse in series three isolated smooth muscle preparations. After passing over the tissues, the blood was collected in a reservoir from whence it returned by gravity to the femoral vein of the dog. (Fig. 1).

The three smooth muscle preparations were a rat stomach strip (Vane, 1957), a chick rectum (Mann and West, 1950) and a rat colon (Regoli and Vane, 1964). The load on the tissues was 1-3 g. Changes in tissue length were detected by auxotononic levers attached to Harvard transducers and recorded on a 3-channel Grass polygraph.

Systemic arterial pressure, left ventricular pressure, right ventricular pressure, cardiac output and electrocardiograms were also continuously monitored in another six-channel Grass polygraph. The results of these haemodynamic studies will be published elsewhere.

The rat stomach strip relaxed to both adrenaline and noradrenaline whereas the chick rectum relaxed to adrenaline and was almost insensitive to noradrenaline (Armitage and Vane, 1964). The rat colon (Regoli and Vane, 1964) was very sensitive to the contractor action of angiotensin II but was relatively insensitive to other substances that are likely to be present in the blood.

Because of their specificity and sensitivity to catecholamines, the combination of a rat stomach strip and a chick rectum provided a convenient and simple means for the continuous assay of adrenaline and noradrenaline in the circulating blood (Vane, 1966). When the release of catecholamines was of short duration, it could be calibrated by giving an intravenous injection of the same catecholamine into the animal. When the release was prolonged, calibrations were made by intravenous infusions.

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RESULTS

When the anterior descending branch of the left coronary artery was occluded, an increase in the concentration of adrenaline was detected in the arterial blood in seven out of nine dogs. The release was detected 2-5 min after occlusion and the release was maintained either continuously or intermittently until the dog died from cardiac arrythmia. An experiment is illustrated in Fig. 2. The assay organs were a rat stomach strip, a chick rectum and a rat colon superfused with femoral arterial blood. Calibration of the tissues with intravenous injections showed that adrenaline (1 μg) relaxed the rat stomach strip and the chick rectum; noradrenaline (3 μg) relaxed only the rat stomach strip. When the left anterior descending artery was occluded, both the rat stomach strip and chick rectum relaxed. The patterns of relaxations of these tissues were similar to those produced by adrenaline. This shows that ouly adrenaline was present in the circulating blood.

Where did the adrenaline come from? In order to find out the source of this substance, the adrenal glands were removed in two dogs. When the anterior descending branch of the left coronary artery was ligated in these animals, both the rat stomach strip and the chick rectum did not relax. Thus, in adrenalectomised dog, adrenaline was not detectable in the arterial blood following occlusion of the anterior descending branch of the left coronary artery. These dogs died within 4-10 min from rapid fall in arterial blood pressure.

In contrast to the results obtained from occlusion of the left anterior descending artery, occlusion of the right coronary artery in six out of eight dogs showed a preferential release of noradrenaline into the circulation. An experiment is illustrated in Fig. 3. The top tracing shows the response of the rat stomach strip, the middle tracing shows the response of the chick rectum and the bottom tracing shows the response of the rat colon. Calibrations by intravenous injections showed that adrenaline (2 μg), noradrenaline (4 μg) and angiotensin II (6 μg) produced typical effects as shown. When the right coronary artery was ligated close to its origin, only the rat stomach strip relaxed; the chick rectum was not affected. Comparison of this response with the known effects of adrenaline and noradrenaline on the assay tissues shows that only noradrenaline was liberated into the arterial blood.

The release of noradrenaline in most dogs was not maintained so that 5-10 min after the occlusion, the assay tissues returned to their original baseline. To confirm that adrenaline was selectively released by occlusion of the left anterior descending artery, this blood vessel was ligated in some dogs after noradrenaline release had stopped. Following the occlusion, there was a discharge of adrenaline into the circulation.

The results of the experiments are summarised in Table I. In nine dogs, ligation of the left anterior descending artery induced the secretion of adrenaline in seven dogs; no catecholamine secretion was observed in two dogs. In contrast, ligation of the right coronary artery showed that noradrenaline was released in six out of eight dogs. Of the remaining two dogs, adrenaline was detected in one and a mixture of adrenaline and noradrenaline was detected in the other.

DISCUSSION

The mechanism of adrenaline release induced by occlusion of the anterior branch of the left coronary artery had been analysed by Staszewska-Barczak (1971). She concluded that the medullary secretion of adrenaline is induced reflexly from stimulation of receptors at the site and boundary of the infarct. The reflex pathway involves vagal as well as extra-vagal pathways and supraspinal structures.

The mechanism of selective release of noradrenaline following right coronary artery occlusion is not known at present. However, high concentrations of noradrenaline are

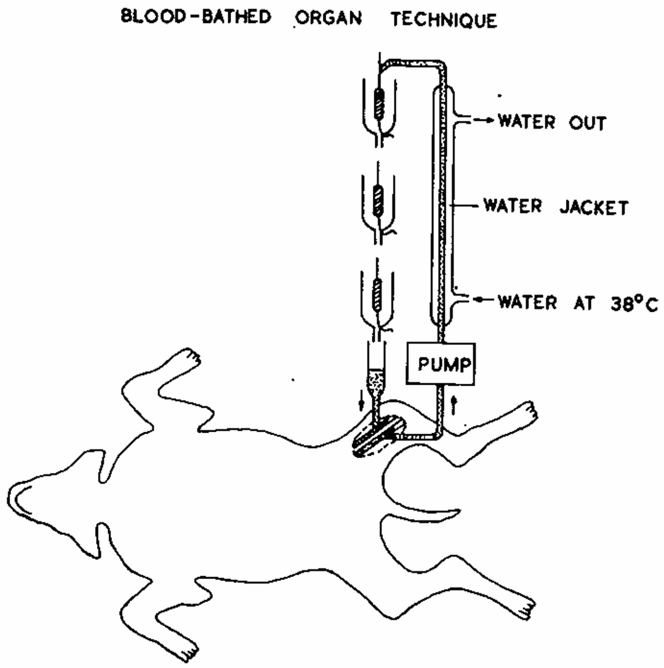

Fig. 1. The blood-bathed organ technique. Heparinised blood from the dog is pumped at a rate of 10 ml/min to superfuse a rat stomach strip, a chick rectum and a rat colon in series. The blood is collected in a reservoir from whence it returned by gravity to the femoral vein. Changes in tissue length were transduced and recorded on a polygraph.

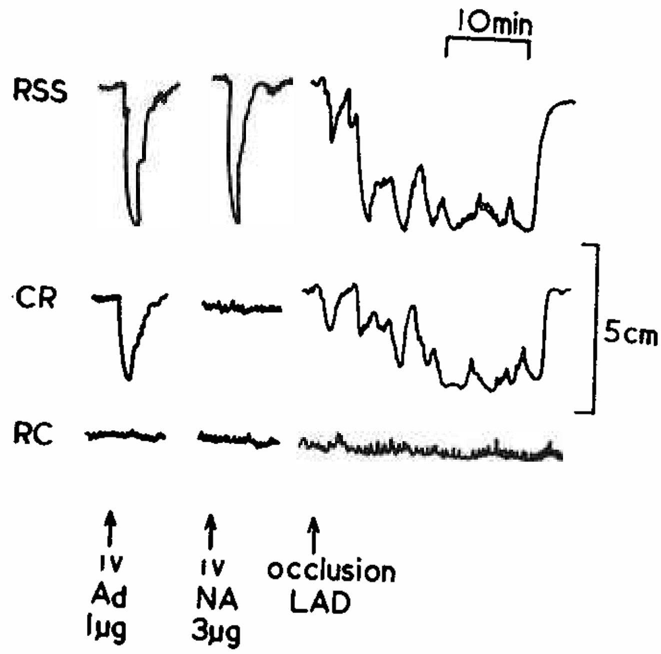

Fig. 2. Release of adrenaline following occlusion of the anterior descending branch of the left coronary artery in a 12 Kg male dog anaesthetised with pentobarbitone. The tracings from top to the bottom show the responses of the rat stomach strip (RSS), chick rectum (CR) and rat colon (RC) to intravenous (i.v.) injections of 1 μg. of Adrenaline (Ad), 4 μg of noradrenaline (NA) and to the occlusion of the left anterior descending artery (LAD). The relaxations of the RSS and CR following occlusion LAD show that adrenaline was released into the circulation. Time, 10 min; vertical scale, 5 cm.

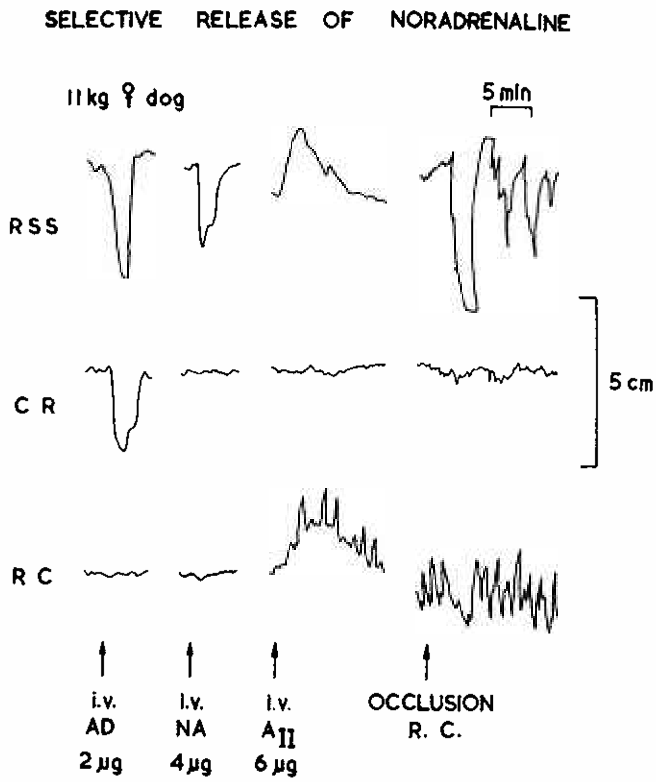

Fig. 3. Release of noradrenaline following occlusion of the right coronary artery in a 11 Kg female dog under pentobarbitone anaesthesia. The tracings from top to bottom show the responses of a rat stomach strip (RSS), chick rectum (CR) and rat colon (RC) to calibrations with intravenous (i.v.) injections of 2 μg of adrenaline (Ad), 4 μg of noradrenaline (NA), 6 μg of angiotensin II (AII) and to the effect of occlusion of the right coronary artery (RC). The marked relaxation of the RSS following occlusion of the right coronary artery shows that noradrenaline was released into the circulation. Time, 5 min; vertical scale, 5 cm.

TABLE I

The selective release of catecholamines following occlusion of the anterior descending branch of the left coronary artery (LAD) and right coronary artery (RC). Occlusion of LAD induced the release of adrenaline in seven out of nine dogs whereas occlusion of the RC induced a release of noradrenaline in six out of eight dogs.

Artery	Number of Dogs				
	Total	Adrenaline release	Noradrenaline release	Ad. & Norad. release	No release
L.A.D.	9	7 (78%)	0	0	2 (22%)
R.C.	8	1 (12·5%)	6 (75%)	1 (12·5%)	0

present in the right atrium and right ventricle in the heart of the dog (Angelakos, 1965). It is conceivable that noradrenaline is released from the infarct area following occlusion of the right coronary artery.

In summary, we have used the blood-bathed organ technique (Vane, 1969) to assay continuously the release of catecholamines into the circulation. Occlusion of the anterior descending branch of the left coronary artery results in the release of adrenaline in seven out of nine dogs whereas occlusion of the right coronary artery results in the release of noradrenaline in six out of eight dogs. This suggests that catecholamines can be sectively released into the circulation by left or right coronary occlusion.

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