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Variation in the response of rats to chemical and thermal injury

G. K. SALMON* and G. B. WEST

Department of Applied Biology, North East London Polytechnic, Romford Road, London, E.15

In 1967, Starr & West showed that a relationship exists between the degree of oedema formation and the amount of bradykinin released when paws of rats were heated. Whilst studying the response of hindpaws of Wistar rats to heat, we noticed that animals from one colony failed to release detectable amounts of kinin yet developed oedema. A comparison was therefore made of the response of two colonies of Wistar rats (Tuck and Ash) to different inflammatory stimuli.

Chemical injury was induced by the topical application of xylene (0·04 ml) to both the foot and the shaved back of rats pretreated with azovan blue dye, and the local inflammatory response was assessed by measuring the amount of protein-bound dye accumulating. Coaxial perfusion of the hindpaw (Rocha e Silva & Antonio, 1960), followed by the application of xylene to the foot, was used to examine the possible release of mediators. The perfusing Tyrode solution was collected and injected on to superfused rat uterus, rat duodenum and guinea-pig ileum preparations (arranged in cascade fashion) to detect histamine, 5-hydroxytryptamine and kinin. Responses of the tissues were recorded isometrically on Devices pen recorders. In other animals, blood pressure changes arising from the topical application of xylene were recorded from the left carotid artery of rats under urethane anaesthesia (1·25 g/kg I.P.). Whereas the hypertensive responses in rats from both colonies were similar, local leakage of dye was markedly greater in the Tuck animals and only in these rats was kinin release detected in the paw perfusate (8 ng average of 4 experiments).

Thermal injury induced by immersing one hindpaw in a water-bath at 50·5° C for 30 min was assessed both by changes in paw volume (recorded on a volume differential meter) and by leakage of dye from the circulation into the subcutaneous tissues. In further experiments, coaxial perfusion of the heated hindpaw was carried out, the perfusate being examined for the presence of mediators, as described above. Blood pressure changes resulting from the thermal injury were also recorded. Rats from the Ash colony responded with a greater oedema reaction and more salivation than did rats from the Tuck colony, although the dye leakage and hypertensive responses were si Correspondingly, kinin release in Ash rats under the heat stimulus (12 ng, average of 4 results) greatly exceeded that in Tuck rats (1 ng, average of 4 results). In no experiment was histamine or 5-hydroxytryptamine detected on the three test preparations.

The results of further experiments using subcutaneous injections of local anaesthetics (e.g. lignocaine, 0·25 mg) showed that, when the thermal responses of rats from both

colonies were unaltered, the xylene responses as well as those to intradermal bradykinin, histamine and 5-hydroxytryptamine, were markedly reduced.

Thus, the response of Wistar rats to chemical and thermal injury varies with the colony used. The present results also show that xylene is capable of releasing kinin. Further experiments are in progress to study the interaction between kinin release by xylene and sensory nerve activation.

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Drug-induced changes in blood flow in normal and ischaemic regions of the canine myocardium

I. MCA. LEDINGHAM, R. J. MARSHALL* and J. R. PARRATT

Department of Surgery, University of Glasgow, Western Infirmary and Department of Pharmacology, University of Strathclyde, Glasgow

Recently it has been shown (Ledingham, McArdle & Parratt, 1972) that carbochromen, an active coronary dilator drug, is incapable of increasing flow in the acutely ischaemic canine myocardium. The purpose of this investigation was to determine whether other drugs, which increase blood flow to the normal myocardium, could improve perfusion in a developing infarct.

Myocardial infarcts were produced in 42 greyhounds, breathing oxygen and 0·5-1·0% trichlorethylene, by acute ligation of the anterior descending branch of the left coronary artery. A catheter inserted distal to the ligature was used to measure peripheral coronary pressure (PCP), retrograde flow (PCF) and infarct flow by the myocardial clearance of ^{133}xenon injected into this catheter. Flow to the normal myocardium was measured with a non-cannulating Nycotron electromagnetic flow probe around the left circumflex artery. The effects, in this experimental model, of five vasoactive substances are summarized in Table 1.

TABLE 1. *Effect of five vasoactive drugs on normal and ischaemic myocardial blood flow in greyhounds, when administered intravenously, 2–3 h after coronary artery ligation (mean ± S.E.)*

Drug	Dose	Normal myocardial blood flow (ml/min) Pre	Normal myocardial blood flow (ml/min) Post	Infarct blood flow (ml/100 g/min) Pre	Infarct blood flow (ml/100 g/min) Post	Effective sub-endocardial driving pressure (mmHg) Pre	Effective sub-endocardial driving pressure (mmHg) Post
Dipyridamole	0·25 mg/kg	68 ±9	132* ±22	20 ±2	15 ±3	8 ±3	5 ±2
Glucagon	50 μg/kg	65 ±11	82* ±16	14 ±1	12 ±3	8 ±2	5 ±4
Isoprenaline	0·4 μg/kg/min	64 ±6	103* ±10	13 ±3	19 ±4	9 ±3	7 ±2
Noradrenaline	1·0 μg/kg/min	79 ±8	145* ±13	18 ±3	40* ±4	3 ±1	16* ±6
Oxyfedrine	0·5 mg/kg	65 ±8	107* ±8	12 ±2	23* ±2	4 ±2	8* ±3

* $P < 0·05$ (paired 't' test)

Neither arteriolar dilatation (dipyridamole) nor myocardial stimulation (glucagon and isoprenaline) increased blood flow in the ischaemic region, although each of these drugs markedly increased flow in the normal myocardium. This is presumably because the vessels in the ischaemic region are near-maximally dilated. Only noradrenaline and oxyfedrine (Ledingham *et al.*, 1972) consistently increased blood flow in the ischaemic region. These were also the only drugs that increased the transventricular perfusion gradient ('effective sub-endocardial driving pressure'; diastolic PCP—left ventricular end-diastolic pressure (LVEDP), Marshall & Parratt, 1973). Noradrenaline achieved this