The relative potencies of adrenaline, noradrenaline and isoprenaline were as follows:

7° C noradrenaline > adrenaline > isoprenaline
18° C adrenaline > isoprenaline >noradrenaline
27° C isoprenaline ⩾ adrenaline > noradrenaline

The response of the heart to adrenaline at 7° C was blocked by phenoxybenzamine or dibenamine, but when the temperature was raised to 24° C, the response was not affected. If the hearts were incubated with these alkylating agents at 24° C and then cooled to 7° C, the response to adrenaline was unaffected.

These results support the postulate of a metabolically influenced receptor in the isolated frog heart, but do not support the concept of a single adrenoreceptor. It is suggested that the change in receptor type is an expression of the relative availability of two separate receptor pools.

REFERENCE

KUNOS, G. & SZENTIVANYI, M. (1968). Evidence favouring the existence of a single adrenergic receptor. *Nature, Lond.*, **217**, 1077–1078.

The effects of carbochromen on myocardial blood flow and metabolic heat production before and after acute coronary ligation

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Using a heated thermocouple technique to measure myocardial blood flow and metabolic heat production (see Grayson & Parratt, 1966), the effects of a methoxycoumarin derivative, carbochromen (Nitz & Pötzsch, 1963; Lochner & Hirche, 1963) have been studied in the normal canine myocardium and in the ischaemic

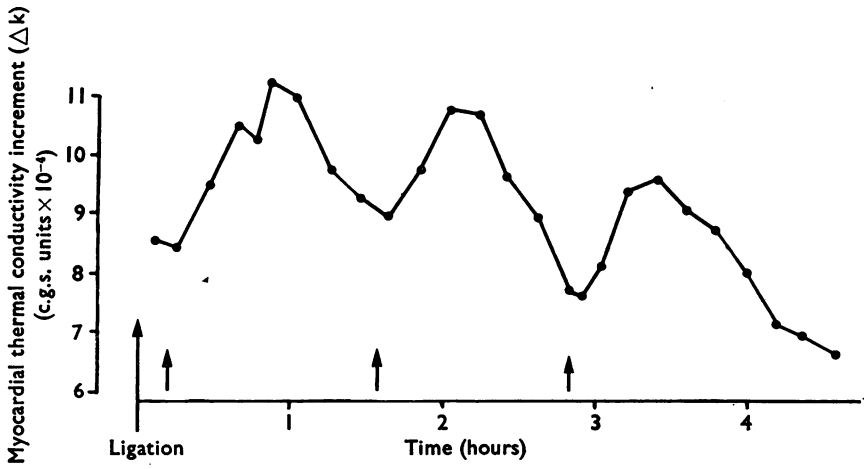

FIG. 1. The effect of intravenous injections of carbochromen (2 mg/kg, at the arrows) on blood flow in the apical region of the myocardium of a dog following acute coronary artery ligation (at time zero). Notice the gradual decrease in baseline flow over the 4 hr period and the fact that carbochromen can markedly increase flow in this developing infarct. Myocardial blood flow expressed as myocardial thermal conductivity increment $\times 10^{-4}$ c.g.s. units.

myocardium (in a developing infarct). Carbochromen (2 mg/kg intravenously) usually increased blood flow in the normal myocardium (myocardial thermal conductivity increment increased from $3{\cdot}3 \pm 0{\cdot}5 \times 10^{-4}$ cal.cm^{-1}.sec.$^{-1}$.°C^{-1} to $5{\cdot}5 \pm 0{\cdot}6$ units; a mean increase of 67%), decreased myocardial vascular resistance from 54 ± 6 arbitrary units to 31 ± 3 units (43%) and depressed myocardial "corrected temperature", an index of metabolic heat production, by $-0{\cdot}22 \pm 0{\cdot}03$° C. These myocardial effects lasted for about an hour. In this dose carbochromen did not influence either systemic arterial pressure or heart rate.

Effects on that part of myocardial energy lost as heat may be a mechanism by which organic nitrites and nitrates, and β-receptor blocking drugs, benefit the anginal patient (Grayson, Irvine & Parratt, 1967; Parratt, 1969). If this is so carbochromen might also be effective in this condition.

Acute ligation of the descending branch of the left coronary artery in dogs causes a marked reduction in local blood flow in the region of the myocardium (apex) supplied by this vessel. This is due to a progressive vasoconstriction leading to a total closure of the microcirculation in about six hours (Grayson & Lapin, 1966; Grayson, Irvine, Parratt & Cunningham, 1968). During this period injections of carbochromen decreased metabolic heat production in the myocardium and were still capable of dilating the vessels of the microcirculation (Fig. 1). We regard this as further evidence that the ischaemia that follows acute coronary occlusion is the result of an active vasoconstriction. The available evidence (Grayson *et al.*, 1968) suggests that this is due to activation of α-adrenotropic receptors in the myocardial microcirculation.

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REFERENCES

GRAYSON, J. & LAPIN, B. A. (1966). Observations on the mechanisms of infarction in the dog after experimental occlusion of the coronary artery. *Lancet*, **1**, 1284–1288.

GRAYSON, J. & PARRATT, J. R. (1966). A species comparison of the effects of changing perfusion pressure on blood flow and heat production in the myocardium. *J. Physiol., Lond.*, **187**, 465–488.

GRAYSON, J., IRVINE, MONA & PARRATT, J. R. (1967). The effects of amyl nitrite inhalation on myocardial blood flow and metabolic heat production. *Br. J. Pharmac. Chemother.*, **30**, 488–496.

GRAYSON, J., IRVINE, MONA, PARRATT, J. R. & CUNNINGHAM, J. (1968). Vasospastic elements in myocardial infarction following coronary occlusion in the dog. *Cardiovasc. Res.*, **2**, 54–62.

LOCHNER, W. & HIRCHE, H. (1963). Untersuchungen mit 3-(β-Diäthylaminoäthyl)-4-methyl-7-carbäthoxy-methoxy-2-oxo-(1,2-chromen), einer neuen coronargefässerweiternden Substanz. *Arzneimittel-Forsch.*, **13**, 251–254.

NITZ, R. E. & PÖTZSCH, E. (1963). 3-(β-Diäthylamino-äthyl)-4-methyl-7-carbäthoxy-methoxy-2-oxo-(1,2-chromen), ein Präparat mit spezifischer und lang anhaltender coronargefässer weiternder Wirkung. *Arzneimittel-Forsch.*, **13**, 243–250.

PARRATT, J. R. (1969). The effect of adrenaline, noradrenaline and propranolol on myocardial blood flow and metabolic heat production in monkeys and baboons. *Cardiovasc. Res.*, **3**, in the Press.

The effect of "selective" beta-receptor blocking drugs on the myocardial circulation

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There is still some doubt as to the nature of the direct effect of the catecholamines on the vessels of the myocardial circulation. Sympathetic amines probably mainly