These degenerative changes were not present in ventricular muscle of four rats subjected to sham operations, or in two adrenalectomized rats which were given replacement therapy with corticosterone.

The ventricular muscle changes observed may account in part for the changes in cardiac function occurring after adrenalectomy.

† Present address: Middlesex Hospital Medical School, University of London.

REFERENCES

RAMEY, E. R. & GOLDSTEIN, M. S. (1957). The adrenal cortex and the sympathetic nervous system. *Physiol. Rev.*, **37**, 155–195.

REMINGTON, J. W. (1951). Circulatory factors in adrenal crisis in the dog. *Am. J. Physiol.*, **165**, 306–318.

SOLOMON, N., TRAVIS, R. H. & SAYERS, G. (1959). Corticosteroids and the functional capacity of the rat heart–lung preparation. *Endocrinology*, **64**, 535–541.

WEINER, D. E., VERRIER, R. L., MILLER, D. T. & LEFER, A. M. (1967). Effect of adrenalectomy on haemodynamics and regional blood flow in the cat. *Am. J. Physiol.*, **213**, 473–476.

Two types of adrenoreceptor in the isolated frog heart

G. A. BUCKLEY and C. C. JORDAN* (introduced by A. KNIFTON), *Department of Pharmacology, University of Liverpool, Liverpool*

Kunos & Szentivanyi (1968), using isolated hearts from frog and rat, showed that alteration of the temperature, and consequently the metabolic milieu, produced an alteration in adrenoreceptor type. The response to the physiological sympathetic transmitter was blocked only by specific β-receptor antagonists at higher temperatures, and only by α-receptor antagonists at lower temperatures. The occurrence of an " equal and separate " block by pronethalol and phentolamine at 22°–24° C in the winter frog heart was also reported. These workers suggest that in the isolated heart there is a single adrenoreceptor which is qualitatively changed by alteration of the metabolic milieu.

The purpose of our experiments was (1) to investigate the concept of a metabolically influenced receptor in the isolated frog heart; (2) to examine the relative sensitivity of the preparation to noradrenaline, adrenaline and isoprenaline at different temperatures, and (3) to determine whether the observed effects are due to changes in a single receptor, or to changes in the relative predominance of two " receptor pools ".

Hearts were dissected from frogs which had been maintained at 5° C for at least one week. The hearts were perfused by a modified Straub method and suspended in Ringer's solution. Contractions were recorded on a kymograph by means of a conventional spring lever. Three temperature ranges (7° C, 18°–22° C and 28° C) were used.

At 7° C, the increased work output of the heart induced by adrenaline ($1{\cdot}6\times10^{-7}$ to 9×10^{-6}M) was blocked by phentolamine, but not by propranolol. At 18°–22° C, both drugs partially blocked the response to adrenaline. At 28° C, propranolol produced a block, whereas phentolamine was ineffective. In all cases the block was reversed by washing.

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

J. GRAYSON†, MONA IRVINE‡ and J. R. PARRATT*, *Department of Physiology, University of Ibadan, Nigeria, and Department of Pharmacology, University of Strathclyde, Glasgow, C.*1

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

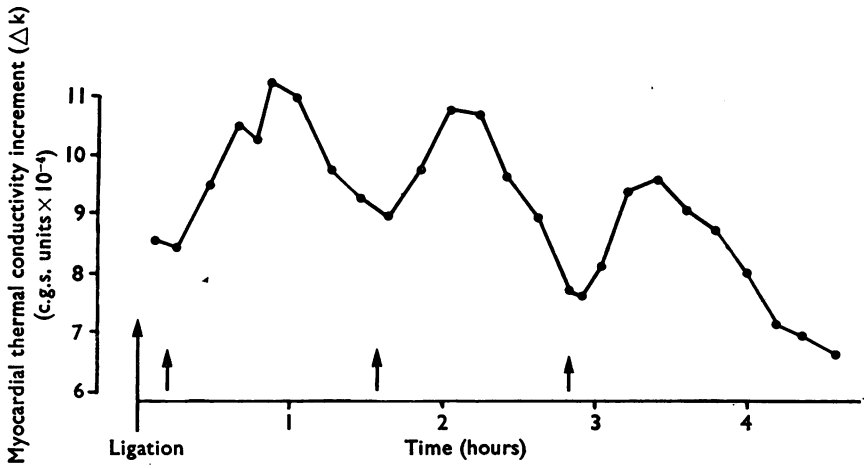

FIG. 1. The effect of intravenous injections of carbochromen (2 mg/kg, at the arrows) on blood flow in the apical region of the myocardium of a dog following acute coronary artery ligation (at time zero). Notice the gradual decrease in baseline flow over the 4 hr period and the fact that carbochromen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