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The influence of adrenocortical insufficiency on cardiac muscle

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In untreated adrenocortical insufficiency the heart is commonly subnormal in size and dry weight (Remington, 1951; Solomon, Travis & Sayers, 1959). No other consistent structural abnormality has been described.

Adrenalectomized animals and Addisonian patients are hypotensive (Ramey & Goldstein, 1957), largely because of a low cardiac output (Weiner, Verrier, Miller & Lefer, 1967). The left ventricular work index of hearts taken from rats adrenalectomized 14 days previously was only 28% of that of controls (Solomon *et al.*, 1959).

Since there are obvious functional changes in the heart after adrenalectomy, we have examined changes in the ultrastructure of the myocardium. Hearts removed from male rats (Wistar) weighing 200–400 g and adrenalectomized 10 days previously were compared with those from sham-operated controls. Adrenalectomized rats were maintained on 0·9% (w/v) NaCl solution.

The mean blood pressures in control and adrenalectomized rats were 120 ± 5 and 101 ± 6 mm Hg ($P<0{\cdot}02$) respectively. Plasma sodium concentration was not significantly different in the two groups (intact $150{\cdot}1 \pm 4{\cdot}6$; adrenalectomized $155{\cdot}3 \pm 3{\cdot}8$ mEq/l.). Plasma potassium concentration (intact, $4{\cdot}59 \pm 0{\cdot}18$ mEq/l.), however, was significantly increased ($P<0{\cdot}001$) in the adrenalectomized rats ($6{\cdot}81 \pm 0{\cdot}28$ mEq/l.). Blood volume in control rats was $8{\cdot}5 \pm 0{\cdot}3$ and in adrenalectomized rats $8{\cdot}3 \pm 0{\cdot}3$ ml./100 g body weight. There were no significant changes in the haemoglobin concentration, the packed cell volume or plasma calcium concentration.

Electron microscopy of pieces of left ventricular muscle showed a patchy disintegration of myofibrils. This process at times extended completely across some cells, adjacent cells remaining normal. Light micrographs of 1 μm sections from the same blocks showed some fibres which stained abnormally pale.

In longitudinal sections, gaps were seen between some filaments; others were no longer parallel, and had a splayed appearance. Particular areas showed extensive loss of both thick and thin filaments but the Z disks were often intact when only a few filaments were present. In some regions myofibrils were completely absent, only granular debris remaining among scattered but apparently normal mitochondria, transverse tubules and sarcoplasmic reticulum.

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.

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Two types of adrenoreceptor in the isolated frog heart

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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.