CONTRACTILE FUNCTION OF THE MYOCARDIUM IN COMPENSATORY HYPERFUNCTION OF THE HEART FOLLOWING ALLOXAN DIABETES

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Meerson's IFS (intensity of functioning of structures) index for the left ventricle in rats with alloxan diabetes under conditions of relative rest is identical with the control value, but is lowered by 15% when the aorta is clamped. In rats with coarctation of the aorta produced against the background of alloxan diabetes, the IFS index falls progressively with repeated compression of the aortic orifice and by the 9th compression is approximately half its level in the control animals.

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In insular deficiency the nuclei acid content and rate of protein synthesis in the myocardium of rats are considerably reduced, while the development of compensatory myocardial hypertrophy during prolonged hyperfunction of the heart is retarded if alloxan diabetes is present [2, 4]. The suggestion has been made that disturbances of nucleic acid and protein metabolism, as well as of energy production during diabetes [7] may lead to weakening of the contractile function of the myocardium.

In the present investigation the contractile function of the left ventricle was studied in animals with alloxan diabetes and in animals with compensatory hyperfunction of the heart caused by experimental coarctation of the aorta superposed on alloxan diabetes.

EXPERIMENTAL METHOD

Experiments were carried out on 33 male albino rats weighing 180-220 g. The animals were divided into four groups: 1) intact, 2) rats with coarctation of the aorta, 3) animals with alloxan diabetes, and 4) rats in which coarctation of the aorta was produced against the background of alloxan diabetes caused by a single subcutaneous injection of 5% alloxan solution in a dose of 18 mg/100 g body weight. The blood sugar was determined by the Hagedorn-Jensen method [1]. Animals whose blood sugar exceeded 300 mg% were used in the investigation. Measured coarctation of the abdominal aorta immediately below the diaphragm was produced by Besnak's method as modified by Kogan [3] four days before the acute experiment. The cross section of the aorta was reduced by about two-thirds. Acute experiments to determine the parameters of contractile function were carried out under urethane anesthesia (160 mg/100 g body weight, intraperitoneally) with the chest opened and under artificial respiration. A polycarbonate cannular connected to a "Barovar" electromanometer, was introduced into the left ventricle through an opening in the apex. The pressure inside the left ventricle, the rate of its change (using a differential circuit) and the ECG were recorded on a type 6 NEK1F_2 apparatus. The index of strength of myocardial contraction was the systolic pressure in the ventricle divided by its weight, the intensity of functioning of structures (IFS) as described by Meerson and Pshennikova [5]. The index of the velocity of contraction was the index of contractility originally suggested by Siegel and Connenblick and modified by Veragut and Krayenbühl [11]. This index was determined by dividing the maximal velocity of development of pressure by the pressure itself in the ventricle at the moment of maximal velocity of pressure development.

At the beginning of the experiment a test was carried out with imposition of an increasing heart rate. Electrical stimulation with pulses 4 V in amplitude and 3 msec in duration was carried out at a frequency

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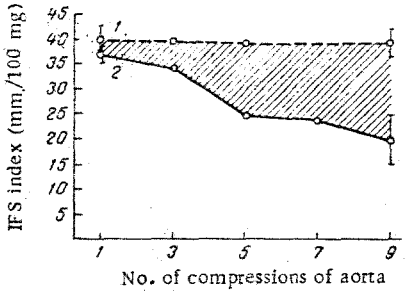

Fig. 1. Dynamics of IFS index for animals with coarctation of the aorta (1) and animals with coarctation of the aorta against a background of alloxan diabetes (2), during repeated compression of the aorta.

slightly higher than the initial heart rate, which was gradually increased to 500 pulses/min. The indices of contractile function were determined 5 min after completion of the test under conditions of relative phyiological rest, and then again with the ventricle working isovolumic conditions, i.e., with the myocardium performing isometric contractions. This situation was created by compressing the ascending aorta for 30 sec during artificial stimulation of the heart at a frequency which was constant in all the experiments.

EXPERIMENTAL RESULTS

During imposition of the artificial rhythm the heart of animals with alloxan diabetes took over the higher rate of contraction with far greater difficulty than the heart of intact rats. For example, a frequency of 440 beats/min, much higher than the spontaneous value, was taken over by 87.5% of intact animals but only 33.4% of animals with alloxan diabetes. In insular deficiency the ability of the heart to reproduce a high frequency of contraction is thus reduced.

In the control animals the initial heart rate was 329 ± 19.6, and remained the same after the 9th compression of the aorta, while in animals with diabetes the heart rate after the first compression was 292 ± 13, and after the 9th compression 235 ± 22, i.e., by the end of the experiment it was reduced by 28% ($P < 0.01$). Consequently, in the course of the experiment the level of automatism characteristic of the spontaneous heart rate was lowered in the animals with alloxan diabetes.

The strength of myocardial contraction under conditions of physiological rest was not significantly different in the animals of the two groups. Under isometric conditions (with compression of the aorta), however, the IFS index of the control animals was 43.2 ± 2.5 and in the animals with diabetes 36.6 ± 1.7 mm/100 mg tissue, i.e., 15% lower ($P < 0.05$). The index of contractility in the experimental rats both at relative physiological rest and under isometric conditions was identical with that in the control animals.

Insular deficiency produced by alloxan administration thus has an adverse effect on contractile function of the myocardium, as is clearly seen when maximal demands are made on the heart. It might be expected that this effect would be more marked during compensatory hyperfunction of the heart caused by coarctation of the aorta.

In animals with coarctation of the aorta but without alloxan diabets the curve showing changes in IFS during repeated compression of the aorta remained at the same level, while the curve for animals in which compensatory hyperfunction of the heart was superposed on alloxan diabets fell fairly steeply, so that by the 9th compression the IFS index was approximately half that of the animals with coarctation of the aorta but without damage to the insular apparatus (Fig. 1). Consequently, in animals with compensatory hyperfunction of the heart against the background of insular deficiency, during repeated loads in the shape of compression of the aorta the maximal strength of contraction fell considerably and fatigue of the myocardium developed rapidly.

The results of these experiments show that in animals with insular deficiency, the strength of contraction of the myocardium under conditions of relative physiological rest is almost indistinguishable from that in control animals, but definitely falls when maximal demands are made on the heart. This is in agreement with the observations of Karlefors [8], who found that the minute volume of the heart in patients with diabetes mellitus is unchanged at rest, but falls appreciably during physical exertion.

In insular deficiency the supply of glucose to the muscle cells is slowed down considerably and the process of its phosphorylation is inhibited [9]. Under these conditions energy formation takes place predominantly on account of increased oxidation of fatty acids [6], which evidently can satisfy to some extent the energy requirements under conditions of physiological rest, but is inadequate in cases when increased cardiac activity is required. In compensatory hyperfunction of the heart, superposed on diabetes, the degree of activation of nucleic acid and protein synthesis in the myocardium is reduced [2, 4], possibly because of inhibition of the stimulant effect of insulin on protein synthesis [12]. On these grounds it is therefore reasonable to suppose that the contractile function of the myocardium is lowered in insular deficiency because of disturbance in the supply of energy-forming and synthetic materials required for physiological function of the myocardial cells.

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