thin, pale cytoplasm, containing few organelles, and with single pinocytotic vesicles. Attention was also drawn to the oriented nature of the changes in cells of the fibroblast series.

During the study of the emergency stage of compensatory hyperfunction of the heart, transformations were observed in vessels of exchange type and in connective-tissue structures. Changes in the structure of the interstitial tissue were probably due to its participation in the formation of adaptive reaction and to the need for a change in the level of transport of metabolites, in the character of the substances transported, and to correction of the composition of the microenvironment of the myocytes. This aspect of the problem may serve as the basis for further investigation of the role of the connective tissue of the heart.

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MORPHOLOGICAL AND FUNCTIONAL FEATURES OF THE LEFT VENTRICLE IN RABBITS WITH EXPERIMENTAL ALCOHOLIC CARDIOMYOPATHY

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Against the background of chronic alcohol poisoning in rabbits a sharp decline is observed in the contractile power of the left ventricle, accompanied by a significant lengthening of the phases of isometric contraction and isometric relaxation. Morphological investigation of the heart revealed marked hypertrophy of the myocardium and intensification of intramyocardial lipolysis, leading to accumulation of acid lipids in the heart muscle. It may be that these lipids, requiring additional quantities of oxygen for their utilization, lead to the appearance of a state of relative hypoxia in the myocardium. Combined with the deficiency of diastole, this may lead to weakening of the contractile power of the heart and to the compensatory development of hypertrophy of the myocardium.

KEY WORDS: cardiomyopathy; alcohol; heart; bioenergetics; lipids.

The mechanisms of development of alcoholic cardiopathy have not yet been adequately explained [1, 2], although this disease is very widespread and accounts for a high percentage

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TABLE 1. Thickness of Muscle Fibers of Left Ventricle in Control and Experimental Animals

	"Pure" control	Water	Pepper	Alcohol
Thickness of fibers, μ	20±0,75	22±0,77	21,3±1,1	33,3±1,5*

Legend. Here and in Table 2, mean values which differed significantly from those of other groups are marked by an asterisk.

TABLE 2. Characteristics of Contractile Function of Heart in Control and Experimental Animals

Index tested	"Pure" control	Water	Pepper	Alcohol
VP_r, mm Hg	105±11	84±11	90±13	54±8*
VP_m, mm Hg	208±6	206±10	196±20	136±12*

of all heart diseases in some countries [10]. It has been shown precisely [3, 4, 6, 7, 9] that in the final stages of this disease marked hypertrophy of the myocardium develops, and against this background severe cardiac failure supervenes. To elucidate the pathogenesis of alcoholic cardiomyopathy it is interesting to study the contractile function of the heart and to compare it with some indices of its metabolism, notably disturbance of the lipid metabolism of the myocardium, for such a disturbance has very serious consequences for the bioenergetics of heart muscle and, consequently, may give rise to changes in the contractile power of the heart.

EXPERIMENTAL METHOD

Experiments were carried out on 40 male Chinchilla rabbits weighing 3.1 kg. A 40% solution of alcohol in a dose of 3.0 ml/kg body weight was given to 10 rabbits daily for 3 days. When this method was used, 2 h after administration of the alcohol its blood level was 0.35± 0.02%. Ten animals received the same quantity of water daily per os for the same period (control); another 10 animals received water together with extract of pepper (control for the stimulating action of alcohol). Another 10 animals formed the "pure control" group. In all the animals 21 days after the beginning of the experiment the real peak intraventricular pressure (VP_r), and the maximal intraventricular pressure (VP_m), recorded during occlusion of the ascending aorta for 5 sec, were determined electromanometrically under acute experimental conditions. Meanwhile the duration of the following phases of the cardiac cycle was calculated: asynchronous contraction (PAC), isometric contraction (PIC), expulsion (PE), and isometric relaxation (PIR). Paraffin sections through the heart muscle were stained with hematoxylin-eosin; cryostat sections were stained with Sudan III and Nile blue sulfate.

All numerical data were subjected to statistical analysis. Differences between means for which $P \leq 0.05$ were taken as significant. Correlation analysis also was carried out on the T1-58 computer.

EXPERIMENTAL RESULTS

By the 21st day of the experiment the animals receiving alcohol developed marked hypertrophy of the heart muscle (Table 1).

Analysis of the contractile function of the heart showed that in animals receiving alcohol there was a significant decrease in both the real and the maximal peak systolic pressures (Table 2).

Correlation analysis showed the presence of strong significant negative correlation ($\rho = -0.956$) between the degree of development of myocardial hypertrophy, reflected in the thickness of the muscle fibers, and the value of VP_m.

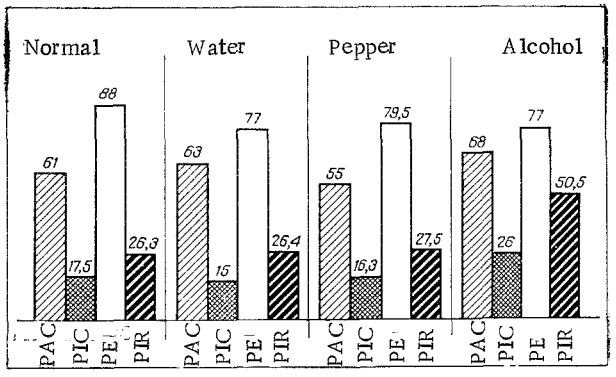

Fig. 1

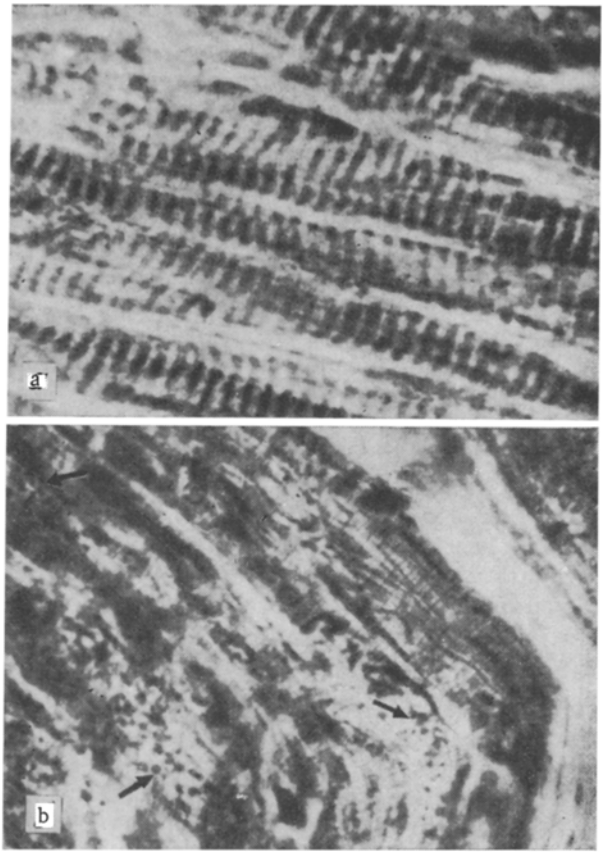

Fig. 2

Fig. 1. Structure of cardiac cycle in control animals and in rabbits with alcoholic cardiomyopathy. Explanation in text. Mean values differing significantly from corresponding values in control groups indicated by + sign. Duration of phases of cardiac cycle given in milliseconds.

Fig. 2. Myocardium of intact rabbit (A) and of rabbit with alcoholic cardiomyopathy (B). Phase contrast. Stained with Nile blue sulfate, 756×. Absence of acid lipid granules in control but they are numerous (indicated by arrows) in the experimental animal.

The study of phases of the cardiac cycle showed that in animals receiving alcohol there was a statistically significant lengthening of PIC and PIR (Fig. 1). No differences in the value of these indices was observed between each of the three control groups. No significant change likewise was observed in PAC and PE in the animals receiving alcohol.

Analysis of the structure of the cardiac cycle also showed that in animals receiving alcohol diastole accounted for 46.7% of the duration of the cardiac cycle (52.7% in the "pure" control; 55.9% in the control with water; 53.7% in the control with pepper extract); moreover, in the animals receiving alcohol strong significant positive correlation was found between this index and the value of VP_m (ρ = +0.911).

In sections through the heart of the experimental animals stained with hematoxylin and eosin, besides signs of hypertrophy of the myocardium no other abnormalities were found. In sections from these rabbits stained with Sudan III and Nile blue sulfate a significant decrease was observed in the content of neutral fat in the hard tissue, with the appearance of numerous granules of acid lipids, hardly any of which are observed in the normal rabbit myocardium (Fig. 2). In the animals drinking pure water and water with pepper extract, no significant differences from normal were found on morphological examination of the myocardium.

These experiments thus showed that in chronic alcohol poisoning hypertrophy of the heart muscle develops and is accompanied by a significant decrease in the contractile power of the myocardium. In the experimental animals PIC and PIR, i.e., energetically dependent phases of the cardiac cycle, were significantly lengthened: Relative shortening of diastole took

place. Intensification of intramyocardial lipolysis and accumulation of acid lipids were observed in the myocardium. The stress situation associated with the drinking process and the stimulating action of the substances administered, had no significant effect on the function or morphological picture of the heart muscle.

The following hypothesis on the mechanisms of formation of the cardiopathy during alcoholic intoxication can be put forward on the basis of these results. Ethanol is known [5] to stimulate production on NAD and to increase its concentration, and this must inevitably intensify hydrolysis of the triacylglycerols and lead to the accumulation of free fatty acids in the body, where they are selectively adsorbed by the myocardium. These acids require extra oxygen for their utilization, so that a state of relative hypoxia may develop in the heart muscle and, in turn, this leads to weakening of the contractile power of the myocardium, for it does not receive sufficient energy. There are also indications [8] that ethanol inhibits the uptake of calcium ions by the sarcoplasmic reticulum, which makes diastole imperfect and aggravates even more the disturbance of contractile activity of the myofibrils. Moreover, in alcohol poisoning diastole is relatively shortened, and this adversely affects resynthesis of energy substrates in the heart muscle and leads to further weakening of the contractile force of the heart. Hypertrophy of the myocardium may develop as a response to this situation, but under conditions of relative oxygen deficiency it will not be sufficiently effective, for because of the increase in weight of the myofibrils, the energy deficiency rises considerably. Conditions are created for the formation of a vicious circle, which is the basis for the formation of alcoholic cardiomyopathy.

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