release from sympathetic terminals through their action on the Ca-dependent mechanism of mediator secretion in the membrane of the nerve ending; 2) PG limit the direct action of CA on effector cells by inhibiting cAMP formation. Considering that extrinsic CA were injected, the second of these mechanisms was evidently predominant in the experimental animals.

It can be concluded from these results that PG, like other stress-limiting systems of the body [4], are factors limiting myocardial damage in adrenalin-induced myocardial dystrophy.

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QUANTITATIVE EVALUATION OF BLOOD SUPPLY OF A FOCUS OF MYOCARDIAL ISCHEMIA IN DOGS IN EXPERIMENTAL PHARMACOLOGY

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To assess the anti-ischemic action of drugs it is very important to have data on their effect not only on the total blood supply to the heart muscle, but also on the blood supply to the actual focus of myocardial ischemia. The reason is that whereas many antianginal drugs do not increase the total blood flow into the heart, and may even reduct it, they redistribute the blood flow in favor of the ischemic zone [9] and, in that way, they improve its functional state.

Most existing methods of evaluating the local and collateral blood flow in a region of myocardial ischemia involve the use of labeled microspheres [10], or measurement of clearance of radioactive isotopes [11] and other substances [1], they are discrete, and some of them do not allow the parameter studied to be assessed quantitatively [8]. Determination of the coronary blood flow in a focus of myocardial ischemia by recording the outflow of venous blood from the ischemic zone involves disturbance of the integrity of the coronary artery or of the vein draining blood from the ischemic focus [5, 12].

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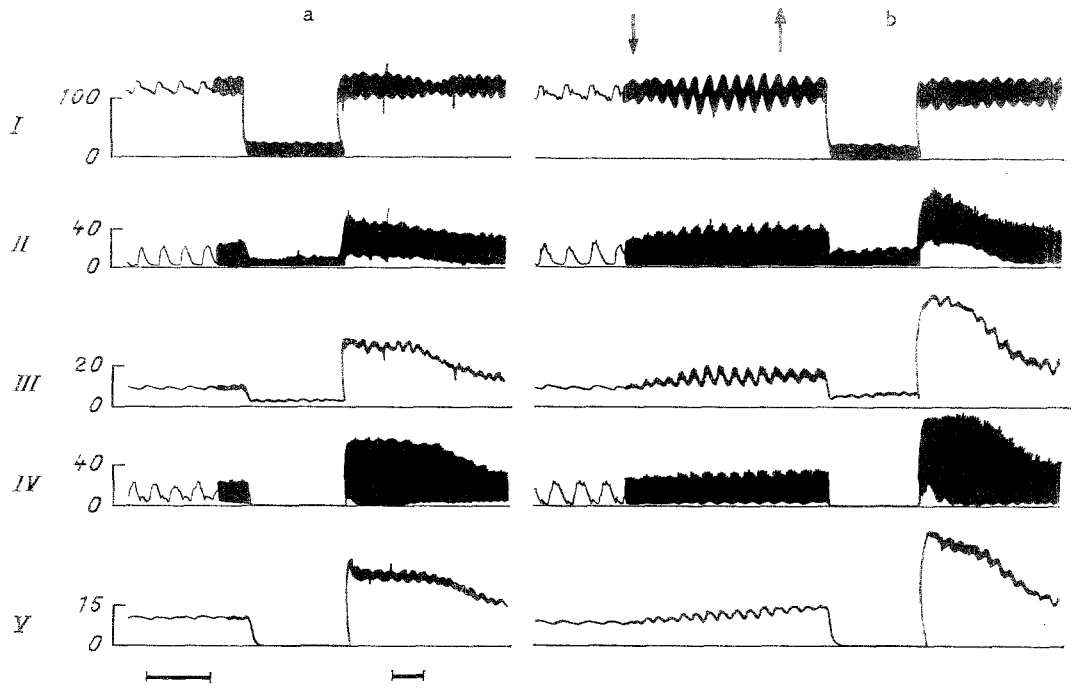

Fig. 1. Effect of sodium hydroxybutyrate on blood flow in zone of myocardial ischemia during acute occlusion of coronary artery in a dog. a) Occlusion after injection of physiological saline (control), b) occlusion after injection of sodium hydroxybutyrate (200 mg/kg, intravenously); I) pressure in coronary artery (in mm Hg), II) phasic blood flow in vein draining zone of myocardial ischemia (in cm/sec), III) mean value of blood flow in vein draining zone of myocardial ischemia (in ml/min), IV) phasic blood flow in coronary artery (in cm/sec), V) mean value of blood flow in coronary artery (in ml/min). Time marker: 1 sec and 1 min. Arrow pointing downward indicates beginning, arrow pointing upward — end of injection of preparation.

EXPERIMENTAL METHOD AND RESULTS

To evaluate the blood supply to an ischemic focus in the myocardium ultrasonic Doppler blood flow transducers were applied to the vein directly draining the ischemic zone. In previous experiments on dogs, the writers used an ultrasonic method to measure blood flow in the circumflex branch of the left coronary artery in acute and chronic experiments [3]. With recent improvements in ultrasonic techniques miniature transducers have been developed, and have been successfully used in investigations of the coronary blood flow in cats [6]. Important conditions for correct measurements when recording the venous blood flow are lightness of the measuring device and high elasticity of its connections. Taking these conditions into consideration transducers have been devised in the form of a bandage 2.0-2.5 mm long with an internal diameter of 1.0 and 1.5 mm. Piezoelectric crystal plates made from TsTS ceramic, 0.2 mm thick and measuring 1.0 × 1.5 mm, were used as ultrasonic sources and sensitive elements. The cable from the transducers was made of thin, high-elasticity multistranded wire with an external diameter of 0.3 mm. The transducers weighed less than 0.25 g. The linear velocity of the blood flow was determined by measuring the frequency of the Doppler signal. To record the volume velocity of the blood flow, the transducers were calibrated in bench tests and experiments on animals. Making the transducers in bandage form results in a constant area of cross-section of the blood vessel and enables calibration to be carried out in units of volume velocity of the blood flow (in ml/min). Good stability of the results was achieved in experiments on rats when the volume velocity of the blood flow was measured in the portal vein [2].

Experiments were carried out on dogs weighing 10-15 kg, anesthetized with pentobarbital sodium (40 mg/kg, intravenously). Under artificial respiration the thorax was opened in the fourth left intercostal space. A segment of the anterior descending branch of the left coronary artery was excised in its middle third, where the occluder was placed, and the ultrasonic

blood flow transducer was located 2-3 cm lower. The anterior descending branch of the left coronary artery is nearly always accompanied by two veins. A small area of the vein was isolated 2-3 mm above the junction of these veins, and the second ultrasonic blood flow transducer was applied to it. The phasic and integral blood flow in the coronary artery and vein were recorded. The blood pressure in the anterior descending branch of the left coronary artery was measured by means of a micromanometer [4], by catheterizing a second-order branch located distally to the site of occlusion. An N-338-6 instrument was used as the recorder.

The scheme of the experiments was as follows. After the blood flow transducers had been placed on the vessels, followed by a pause of 30 min (to allow stabilization of the background values), test occlusion of the coronary artery for 1 min was carried out, followed by reperfusion for 30 min. At the 6th minute after intravenous injection of 3 ml of physiological saline over a period of 3 min (at the rate of 1.0 ml/min), the coronary vessel was subjected to control occlusion for 3 min, followed by reperfusion for 30 min. Later sodium hydroxybutyrate was injected intravenously in a dose of 200 mg/kg and experimental occlusion and reperfusion of the coronary vessel were carried out. We chose sodium hydroxybutyrate as a compound which stimulates the collateral coronary circulation [7].

The trace of one experiment involving occlusion of the coronary artery for 3 min before (a) and after (b) injection of sodium hydroxybutyrate in a dose of 200 mg/kg is shown in Fig. 1.

Experiments on six animals showed that sodium hydroxybutyrate considerably increased the blood supply to the focus of myocardial ischemia. Whereas in the control the blood flow in the focus of ischemia 30 sec and 3 min after occlusion of the coronary artery was 5.4 ± 1.9 and 5.9 ± 1.8 ml/min respectively, as a result of the action of sodium hydroxybutyrate it was increased by 53.7 ± 13.3 and 34.1 ± 9.0% respectively ($p < 0.05$). The linear velocity of the phasic blood flow was 7.2 ± 3.0 cm/sec 30 sec after occlusion and 12.9 ± 2.5 cm/sec 3 min after occlusion. After administration of hydroxybutyrate this parameter rose by 60.3 ± 14.7 and 23.2 ± 8.1% ($p < 0.05$) respectively.

By the use of an ultrasonic technique it is thus possible to record the outflow of blood from the focus of ischemia continuously without damage to the vessel wall, and to obtain a complete picture of the action of a drug continuously on the blood supply of the ischemic myocardium. There is no disturbance of the hemodynamics in the ischemic focus in this case: the blood flow in the territory of distribution of the occluded artery continues in its natural direction and no additional ischemia is created as a result of blood sampling.

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