on the pumping function of the heart was studied. Dependence of changes in the cardiac index on the number of microspheres immobilized in the left ventricular myocardium is shown in Fig. 3. A significant decrease of the cardiac index was observed only after about 150,000 microspheres/g had entered LV. In this series of investigations strong correlation was not found between the decrease in basic contractility of LV and the number of microspheres deposited in LV ($r = 0.31$), which can be explained by the action of regulatory mechanisms, on account of which this parameter can remain unchanged even in the presence of relatively large lesions of LV. It was shown, for instance, that the basic hemodynamic parameters are reduced in rats with chronic myocardial infarction if weight of the infarcted zone of the myocardium exceeds 46% of the weight of the left ventricle [8]. Meanwhile relatively strong correlation was found between changes in the contractility index and changes in the cardiac index.

The results show that the model described above can be used to induce measured ischemization of the myocardium in small animals, so that it can be used to study the pathophysiology of acute myocardial ischemia and, for example, to study the relationship between changes in myocardial contractility and the pumping function of the heart, and also for the screening of new therapeutic substances for the treatment of this pathology.

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PHARMACOLOGICAL AND HYPOTHERMIC SUPPORT FOR EXPERIMENTAL DRY HEART OPERATIONS

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The method of no-perfusion hypothermic protection of the patient against hypoxia during operations on the dry heart has already proved its worth in clinical practice. A combination of pharmacological and hypothermic support enables the circulation to be arrested for 30 min or longer, thus providing conditions for the correction of complex heart defects [2]. However, improvement of the method cannot be achieved without an experimental model enabling the various aspects of hypothermia to be studied.

Most experimental investigations of the heart during hypothermia have been carried out on the isolated organ, a heart-lung preparation [3, 4, 8, 12], or an animals cooled with the aid of an artificial circulation apparatus [10, 11]. There have been only a few investigations

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involving whole-body external cooling of dogs [1, 3, 7, 9, 14] and fewer still involving reheating after occlusion of the main vessels under these conditions [1, 6, 13]. There has been no attempt to concentrate attention on the anesthesiologic support for experiments, and information on the complications arising during hypothermia is scanty and requires verification. Some workers [4, 5] state that during cooling below 26°C cardiac activity is inhibited, as is reflected in arrhythmias and intractable fibrillations.

The writers have developed a method of pharmacological and hypothermic support for long-term occlusions in dogs, particular attention being paid to the character of the anesthesiologic support for hypothermia, so that at each dose of the experiment an adequate hemodynamics could be maintained.

EXPERIMENTAL METHOD

Dogs weighing 9-15 kg received premedication, 1 h before the beginning of the operation, in an individual cage, by subcutaneous injection of trimeperidine in a dose of 28-35 mg/kg and a 0.1% solution of atropine sulfate in a dose of 0.05 ml/kg body weight. The dog was then taken into an operating theater, where general anesthesia was induced with pentobarbital in a dose of 10 mg/kg. After incubation of the trachea, basal anesthesia was induced with a mixture of ether and oxygen. Before thoracotomy the anesthesia was deepened with pentobarbital (10 mg/kg) to stage III_I, thoracotomy was performed, and the main vessels were mobilized. The dog was cooled in a bath by wetting the whole surface of the body with water (0-4°C) and covering it with finely crushed ice and snow. The rate of cooling averaged 1° in 5-7 min. Active cooling ended when the rectal temperature was 28°C, and the body temperature was lowered further to 26°C passively. During the cooling period, a muscle relaxant was administered by drip in a dose of 1 mg/kg in 100 ml of 5% glucose solution, and heparin was given fractionally in a dose of 75 U/kg to prevent blood clotting and to improve the microcirculation. An intravenous injection of 8-10 mg/kg of prednisolone was given 5 min before the heart was disconnected from the blood flow. The main vessels were occluded by compressing consecutively the inferior and superior venae cavae and the aorta; the artificial lung ventilation apparatus was disconnected at this time. To stop the heart quickly, 5 mg/kg of Bunyatyan's cardioplegic solution (5% glucose solution — 400 ml, 7.5% potassium chloride — 8.0 ml, 4% sodium bicarbonate — 10 ml, 25% magnesium sulfate — 3.0 ml, heparin — 0.4 ml; 2-4°C) was injected into the root of the aorta. To stop fibrillations if they developed, the heart was subjected to additional external cooling with finely crushed ice and the temperature of the myocardium was maintained at about 16°C during the first 15 min of occlusion. The ice was then removed, and toward the end of occlusion the temperature was raised passively to 17-18°C. The total duration of occlusion was 35 min or more. The artificial lung ventilation apparatus was connected 30 sec before the end of occlusion, after which the clamps were removed and resuscitation commenced: direct cardiac massage, heating heart with warm (35-40°C) physiological saline and, if necessary, intravenous injection of cardiac tonics and defibrillation. After restoration of cardiac activity the dog was reheated sternally with warm (45°C) water. The rate of reheating was 1° in 10-12 min. Under these circumstances the pentobarbital anesthesia was deepened by administration of 4-5 mg/kg. Depending on the circumstances, the hemodynamics was maintained by fractional injection of 0.1 mg/kg of phenylephrine. When the body temperature reached 35-36°C, the thorax was sutured without drainage and the ether disconnected.

EXPERIMENTAL RESULTS

Operations by the method described above were performed on 24 dogs. The mortality for various technical reasons was 18%. The postoperative period was uncomplicated. No evidence of neurologic disorders was found. Toward the end of the 3rd day the state of the animals was quite satisfactory: they ate, drank, urinated, and moved about quite independently. No visible pathology of the heart or other internal organs could be found in dogs killed on the 3rd day with the exception of signs of natural aseptic reactive inflammation at the sites of the surgical procedures.

The suggested scheme of anesthesiologic support for experiments on the dry heart was used with minimal variations for occlusions lasting 15 min, under conditions of general, moderate hypothermia (28-30°C), for occlusions lasting 60 min with a body temperature of 21-24°C, and during deep general hypothermia of animals to 16°C followed by reheating.

The ability to ensure reversible, prolonged periods of a dry heart during no-perfusion hypothermia, with appropriate anesthesiologic support in dogs enables new surgical operations

to be developed experimentally, including organ transplantation. The suggested method can also be used for further research into the longest possible duration of circulatory arrest against the background of different levels of hypothermia, for testing drugs with protective properties (membrane stabilizers, for example). The study of the phenomenon of hypothermic protection itself and of its different components, by a comprehensive study of animals in the course of the experiment (recording temperature in different parts of the body, the blood pressure, ECG, spirogram, and taking samples of blood and biopsy material from different parts of the heart for various investigations) is no less important. A particularly valuable feature of this experiment is that recovery and regeneration processes can be observed in the late stages, which is impossible, in principle, in clinical practice, but is of great practical importance.

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