ACCESSORY CIRCULATION IN EXPERIMENTAL MYCARDIAL ISCHEMIA AND THE ENERGY METABOLISM OF THE HEART

Yu. G. Novikov, E. G. Bykov
L. V. Tkacheva, and G. T. Mineeva

UDC 616.127-005.8-092.9-089 : 616.124.2-089.
856.168 : 616.12-092.612.013.7

An extracorporeal circulation is used nowadays to compensate disturbances of the hemodynamics [10]. Salisbury [9] observed that the accessory circulation, working on the principle of shunting the left ventricle, leads to complete compensation even of severe circulatory failure caused by disturbances of the coronary blood flow.

In the present investigation a study was made of the oxygen balance of the heart and the carbohydrate balance and concentration of high-energy phosphorus compounds in the mycocardium after high ligation of the anterior descending branch of the left coronary artery, followed by shunting of the left ventricle in dogs [5].

The experiments were carried out on 74 noninbred dogs weighing 15-25 kg.

EXPERIMENTAL METHOD

The main experiments were carried out on 25 animals anesthetized with morphine and thiopental and maintained on controlled respiration with oxygen. The coronary sinus was catheterized and the volume velocity of the blood flow determined by means of an electromagnetic relay. Blood samples were taken through the same catheter.

Samples of arterial blood were obtained through a catheter introduced into the carotid artery. A platinum electrode for recording the oxygen tension on a polarograph was inserted into the mycocardium of the anterior wall of the left ventricle in the zone supplied by the descending branch of the left coronary artery. The descending branch of the left coronary artery was isolated in its upper third and ligated. Twenty minutes later the left atrium was catheterized through the oricle by a catheter 8 mm in diameter, a cannula was introduced into the left femoral artery, and the NIIEKhAiI artificial circulation apparatus without an oxygenator was connected to it. Shunting of the left ventricle began 30 min after ligation of the coronary artery or sooner (in cases of cardiac arrest), and continued for 30-45 min. To prevent the blood from clotting heparin was injected. The left ventricle was partially and completely excluded from the circulation.

In blood samples taken at different times of the experiment the oxygen concentration was determined by Van Slyke's method, the glucose concentration by the anthrone method, the pyruvate level by a colorimetric method with salicyl aldehyde and the lactic concentration by the Barker — Summerson method. In 15 acute experiments the heart was extracted 15 min after the end of shunting. In 10 acute experiments, the heart was extracted 15 min after the end of shunting. In 10 chronic experiments, the operation was concluded by suturing the chest wall. These animals were again anesthetized 3 or 24 h after ligation of the artery and the heart was extracted for examination. The components of the adenyl system in the parts of the heart muscle from the zone of ischemia and from the posterior wall of the left ventricle were investigated by paper chromatography, the creatine phosphate was estimated by A. M. Alekseeva's method, and glycogen by A. L Shabadash's method [6]. The ATPase activity of the mycocardium was determined by the method of Wachstein and Meisel [12], and by the calcium method of Padykula and Herman [8].

Central Research Laboratory and Department of Biochemistry, Voronezh Medical Institute. Scientific Director or Research Professor T. S. Lavorva (Presented by Active Member of the Academy of Medical Sciences of the USSR, S. E Severin). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 64, No. 7, pp. 30-34, July, 1967. Original article submitted February 18, 1965.

TABLE 1. Concentration in Arterial Blood and Arterio-Venous Coronary Difference (AVCD) of Glucose, Pyruvate, and Lactate (mg %), M±m

	Before ligation of coronary artery		15 min after ligation of coronary artery		30 min after beginning of shunting of left ventricle		15 min after end of shunting of left ventricle	
	in artery	AVCD	in artery	AVCD	in artery	AVCD	in artery	AVCD
Glucose	92,2±6,4	+(3,9±1,1)	90,3±6,1	—(3,6±1,1)	99,0±6,8	+(7,1±1,8)	92,0±5,2	+(5±1,5)
Pyruvate	0,88±0,03	+(0,1±0,01)	0,75±0,08	—(0,06±0,02)	0,9±0,06	+(0,04±0,03)	0,9±0,04	+(0,09±0,01)
Lactate	15±0,8	+(3±0,9)	14±0,9	—(1±0,5)	14,6±1	+(1,2±0,7)	15±1,2	+(2,9±0,7)

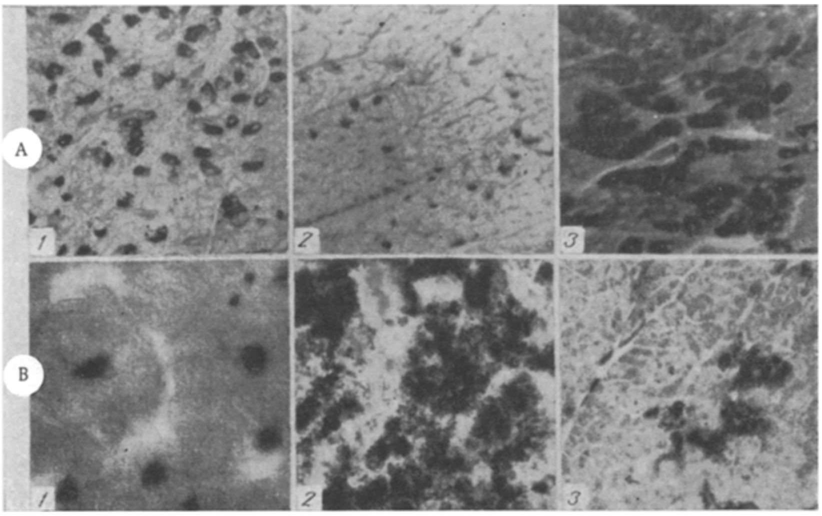

Fig. 1. Glycogen content (A) and ATPase activity (B) in mycocardium of left ventricle. A: 1) Heart of a healthy dog; 2) zone of ischemia 30 min after ligation of the coronary artery; 3) subepicardial area of the zone of ischemia 60 min after ligation of the coronary artery and subsequent shunting of the left ventricle, magnification 10 × 40. B — 1) Heart of a healthy dog (enzyme activity in nuclei, magnification 10 × 90); 2) heart of a healthy dog after shunting of left ventricle (mitochondrial enzyme activity, magnification 10 × 40); 3) zone of ischemia 60 min after ligation of the coronary artery followed by shunting of the left ventricle.

In 29 control experiments, the coronary artery was ligated at the same level but without shunting of the left ventricle. In 10 experiments, the left ventricle was shunted without ligation of the coronary artery; the hearts of 10 healthy dogs were investigated.

EXPERIMENTAL RESULTS AND DISCUSSION

After ligation of the coronary artery the blood flow in the coronary sinus fell on the average by 42%. Despite the increase in the coronary arteriovenous oxygen difference, the oxygen consumption by the heart per minute was reduced. The oxygen tension in the zone supplied by the ligated artery fell to 50 — 10% of its initial level. The glucose utilization from the coronary blood diminished and in most experiments its balance became negative. The pyruvate and lactate balance likewise became negative (see Table 1).

During shunting of the left ventricle the coronary blood flow changed to a varied degree. In 7 experiments in which the blood flow diminished significantly after ligation of the coronary artery, it increased. In the remaining 8 experiments after ligation of the coronary artery the blood flow in the coronary sinus showed only a very slight fall. In these experiments, the blood flow diminished during shunting of the left ventricle. The accessory circulation usually led to a decrease in the oxygen consumption by the heart tissues, both per milliliter of blood flowing through the heart and per unit time. The oxygen tension in the zone of ischemia in these circumstances usually increased slowly (11 experiments), on the average by 35%, while in two experiments it remained at the same level and in another two it fell slightly. During shunting of the left ventricle of the healthy dogs the oxygen tension in the mycocardium often rose above its original level.

The utilization of glucose, pyruvate, and lactate increased during shunting carried out after ligation of the coronary artery, and their balance once again became positive (see Table 1).

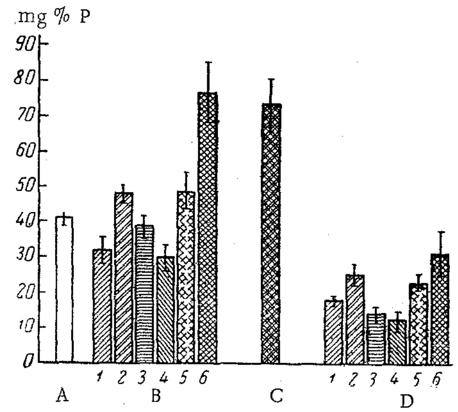

Fig. 2

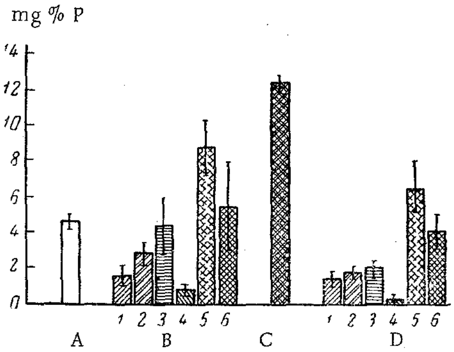

Fig. 3

Fig. 2. Content of ATP in the muscle of the left ventricle (in mg % phosphorus). A — Myocardium of left ventricle of healthy dogs; B — myocardium of posterior wall of left ventricle after ligation of coronary artery; C — myocardium of left ventricle of healthy dogs after shunting of left ventricle; D — myocardium of anterior wall of left ventricle of dogs after ligation of coronary artery (zone of ischemia). 1) 10 min, 2) 30 min, 3) 60 min, 4) 3 h after ligation of coronary artery in control experiments, 5) 60 min, 6) 3 h after ligation of coronary artery and shunting of left ventricle. The lines inside the columns denote the mean error (m).

Fig. 3. Content of creatine phosphate in muscle of left ventricle. Legend as in Fig. 2.

The results of the control experiments showed that in the zone of ischemia 30 min after ligation of the coronary artery an area not containing glycogen was constantly present; this area was smaller than the zone of ischemia. The effect of the accessory circulation was seen first in the part of the myocardium containing glycogen. Granular forms of the carbohydrates appeared in this area in practically all the myocardial fibers, whereas in the myocardium of the healthy intact dogs glycogen was present only in the sarcoplasm of individual cells (Fig. 1A).

Results reflecting the concentration of ATP in the myocardium following ligation of the coronary artery [1-4], shunting of the left ventricle, and ligation followed by shunting [5] are given in Fig. 2. In the first 10 min of ischemia, a decrease in the ATP content was observed in the zone of ischemia and the posterior wall of the left ventricle. A tendency toward an increase in the ATP content appeared 30 min later both in the ischemic area and in the area with a normal blood supply. The ATP in the zone of ischemia 1 and 3 h after ligation of the artery progressively diminished. In the experiments with shunting of the left ventricle a statistically significant increase in the ATP content in the zone of ischemia compared with the control was observed in the experiments with something of the left ventricle 1 and 3 h after ligation of the coronary artery ($P < 0.01$). The ATP content in the posterior wall of the left ventricle was much higher than normal. During shunting of the left ventricle of the healthy dogs the ATP content in the anterior and posterior walls of the left ventricle was much higher than normal. Similar changes were found in the CP content (Fig. 3), and also in the content of AMP and ADP.

By means of histochemical methods, from certain forms of ATPase activity of the myocardium in the heart of the healthy dogs, the localization of activity could be detected in the nucleoli and in the capillary endothelium. After ligation of the coronary artery a decrease in ATPase activity was observed, and it disappeared completely after 24 h. Shunting of the left ventricle led to the appearance of ATPase activity in the mitochondria (Fig. 1B) throughout the thickness of the wall of the left ventricle; in these circumstances no ATPase activity was found in the nucleoli. An increase in the ATPase activity of the mitochondria was also observed in the zone of ischemia, but there it was focal in character in contrast to the universal increase in the heart with the normal blood supply.

It may be concluded from these results that the energy metabolism in the zone of acute myocardial ischemia is improved by shunting of the left ventricle.

This may be explained by the decrease in the contractile function of the myocardium of the left ventricle as a result of exclusion of the ventricle from the circulation and by the improvement of its collateral circulation [5]. V. S Shapot and G. M. Pruss showed that the ATP requirement of the heart is directly proportional to its functional load [7]. This state of affairs may evidently apply also to the other components of the energy metabolism. If the contractile power of the muscle of the left ventricle is lowered by excluding it from the circulation, the energy requirements of the myocardium may lead to some degree of conformity with the reduced blood flow in it. Despite the decrease in the oxygen consumption during shunting, the utilization of pyruvate and lactate was increased, suggesting depression of the glycolytic processes. The increase in ATP resynthesis evidently took place on account of an increase in the intensity of oxidative phosphorylation, for the reserves of anaerobic resynthesis of ATP (CP and glycogen) were not reduced while the ATPase activity of the mitochondria increased.

LITERATURE CITED

1. A. V. Vinogradov, in the book: The Physiology and Pathology of the Circulation and Respiration [in Russian], Moscow (1960), p. 7.
2. A. I Kolotilova, S. N. Lyslova, V. K Vagner, et al., Vopr. Med. Khimii, No. 5, 70 (1965).
3. K. S. Mitin, Arkh. Pat., No. 1, 40 (1965).
4. A. L. Myasnikov, Atherosclerosis [in Russian], Moscow (1960).
5. Yu. G. Novikov and V. S. Kharin, in the book: Problems of the Collateral Circulation from the Functional-Anatomical and Clinical Aspects [in Russian], Ivanov-Frankovsk (1964), p. 70.
6. A. L. Shabadash, Izv. Akad. Nauk SSSR, Seriya Biol., No. 6, 745 (1947).
7. V. S Shapot and G. M. Pruss, Dokl. Akad. Nauk SSSR, 108, No. 5, 899 (1956).
8. H. A. Padykula, E. Herman, J. Histochem. Cytochem., 3 (1955), p. 170.
9. P. T. Salisbury, G. E. Cross, P. A. Rieben, et al., Circulat. Res., 8 (1960), p. 431.
10. J. H. Stuckey, et al., Surg. Forum, 8 (1957), p. 342.
11. A. Szent-Györgi, in the book: Advances in Cardiology [Russian translation], Moscow (1959), p. 20.
12. M. Wachstein, E. Meisel, and A. Niedzwiedz, J. Histochem. Cytochem., 8 (1960), p. 387.