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# EFFECT OF AN EXCESSIVE OXYGEN SUPPLY ON MYOCARDIAL ENERGY EXPENDITURE

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KEY WORDS: myocardium; oxygen supply.

It is generally considered that the oxygen consumption of the tissues is independent of their oxygen supply, provided that the partial pressure of oxygen within the tissues remains above a certain critical level, which is very low (of the order of 0.1 kPa). However, there are frequent reports in the literature that the oxygen consumption of skeletal muscles and the myocardium rises in response to an increase in the flow of blood or fluid replacing it through the tissue, i.e., when the oxygen supply is increased while at rest or while the level of activity of the organ remains constant [4-8, 10-15]. If these observations are correct, they demand a substantial re-examination of established views on the course of oxidative processes involving oxygen. They are particularly interesting for cardiology, in which the energies of the heart muscle and its oxygen supply are central problems.

Invesitgations have been undertaken in the writers' laboratory using a method of measuring oxygen consumption by the isolated perfused rat heart. Isolation of the organ modifies the conditions of its activity sharply, but allows the oxygen supply to the tissues to be changed at will and to be monitored sufficiently accurately, a matter of the utmost importance for the solution of problems connected with the influence of oxygen supply on energy metabolism. The problem of the influence of oxygen supply on the energetics of the heart has already been examined by the writers previously [2, 3].

In the investigation descxribed below the range of changes in the oxygen supply of the heart was widened and lactate formation in the heart also was measured at different levels of oxygen supply.

## METHODS

To simplify interpretation of the results, experiments were carried out on the arrested heart. The basis of the experimental method was described previously [1, 2].

The isolated rat heart was perfused at 37°C with Krebs–Henseleit bicarbonate buffer saturated with a mixture of 95% $O_2$ and 5% $CO_2$. The partial pressure of oxygen in perfusion fluid flowing toward the heart was 78-92 kPa. The heart, arrested by excess of potassium, was perfused retrogradely. In each experiment oxygen consumption was calculated only once (3-7 min after cardiac arrest), for the oxygen consumption of the arrested heart changes with time. The rate of perfusion varied from one experiment to another between 40 and 143 ml/g dry weight of myocardium (from now on the parameters are always expressed relative to dry weight of the myocardium) per minute by varying the hydrostatic pressure (7-17 kPa). The rate of lactate formation by the heart was determined in a special additional series of experiments.

The perfused heart was placed in a special chamber connected with two continuous-flow polarographic cells, one of which was placed on the path of inflow of the perfusion fluid into the organ, the other on the outflow path of perfusion fluid, having passed through the

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TABLE 1. Energy Power of Glycolysis in Response to Changes in Oxygen Supply of the Arrested Heart

| $Q_{O_2}$, ml/(g·min) | $P_E$, mW/g | n | P |
|---|---|---|---|
| 0,2—0,6 | 3,4±1,0 | 7 | — |
| 0,7—1,3 | 2,8±1,1 | 8 | >0,5 |
| 1,4—2,6 | 4,1±1,4 | 8 | >0,5 |

Legend. Mean values and standard errors are shown; n) number of measurements, P) probability of significance of difference from power of glycolysis with an oxygen supply of 0.2-0.6 ml/(g·min).

vessels of the organ. The partial pressure of oxygen in the inflowing and outflowing perfusion fluid was measured continuously in these cells. The rate of flow was determined from the time required to fill a measuring burette. Samples of outflowing perfusion fluid were analyzed for their lactate concentration [9]. Oxygen consumption was calculated from the $pO_2$ difference in inflowing and outflowing fluid and the volume velocity of perfusion. The energy power of respiration ($P_E$), in milliwatts per gram, was calculated from the mean energy equivalent of $O_2$, which is 20.4 J/ml. The power of glycolysis was calculated in the same units from the lactate concentration inthe outflowing fluid, the volume velocity of perfusion, and the energy equivalent of lactate formation (94 J/mmole).

The oxygen supply of the oxygen ($Q_{O_2}$), in milliliters of oxygen per gram per minute, was calculated as the product of the oxygen concentration in the inflowing perfusion fluid (proportional to the corresponding $pO_2$), and the volume velocity of perfusion. To assess the adequacy of the oxygen supply, attention was concentrated on the value of $pO_2$ in the "venous" perfusion fluid and the rate of lactate formation.

This paper describes the results of experiments on 49 heart preparations.

## RESULTS

From 3 to 7 min after cardiac arrest, with an increase in oxygen supply from 0.75 to 3.0 ml/(g·min) the oxygen consumption and energy power of respiration increased from 303 to 720 μl $O_2$/(g·min) and from 103 to 245 mW/g respectively. Dependence of oxygen consumption on its supply was observed throughout the range of oxygen supply investigated, and was close to linear. The rate of glycolysis in the myocardium over the whole range of changes in oxygen supply did not change statistically significantly (Table 1). The average rate of lactate formation was 2.9 μmoles/(g·min), which corresponds to 3.4 mW/g, i.e., 2% of the mean level of the total energy consumption of the arrested heart. In three of seven experiments, with an oxygen supply of more than 0.9 ml/(g·min) no lactate whatever was found in the outflowing perfusion fluid, although the oxygen consumption increased in response to an increase in oxygen supply in these cases also.

Dependence of the myocardial oxygen consumption on its oxygen supply which we observed could be explained most easily by the existence of hypoxia of the muscle and a gradual reduction of hypoxia with an increase in oxygen supply. To what extent is this hypothesis true?

First, $pO_2$ in the outflowing (venous) perfusion fluid was 47-70 kPa (350-525 mm Hg), evidence of the considerable oxygen reserve in the outflowing fluid and the good conditions for oxygen diffusion from capillaries into the tissues. Second, evidence against hypoxia is given by the very low lactate concentration in the outflowing fluid and the absence of correlation between the respiration rate and the rate of glycolysis in response to a change in oxygen supply.

Consequently, the myocardium is in fact capable of increasing its oxygen consumption and the energy of its respiration in response to an increase (excess) in its oxygen supply. Since the heart muscle does not perform mechanical work under these circumstances, and the energy capacity of the ADP—ATP, CP system under resting conditions is small, it can be

tentatively suggested that the additional energy of respiration is utilized for nonphosphorylating oxidation and is slowly dissipated in the dissues in the form of heat.

Further investigations are needed for a complete explanation of the physiological significance of the correlation between respiration rate and oxygen supply. The conditions under which this relationship was observed were far from physiological. Although it has been reported that a similar relationship was observed in response to an increase in the coronary flow under physiological conditions [5, 6, 14], these reports require verification. However, it is clear even now that the view that oxygen consumption is independent of supply is not true under all conditions. Oxygen consumption may depend on oxygen supply when the tissue oxygen consumption is unchanged.

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## MYOCARDIAL METABOLISM ON INDUCTION AND PROLONGATION OF ARTIFICIAL HYPOBIOSIS


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Disturbances of cardiac activity occupy a leading place among disorders of the vital functions of animals and man exposed to deep hypothermia [3, 6, 7, 10]. Basic factors in the pathogenesis of these disturbances are changes in energy metabolism of the myocardium [8, 10]. Mobilization of energy-yielding substrates and stimulation of the initial stages of their utilization under the influence of cold on the body are largely determined by the activating influence of the sympathicoadrenal system [6, 10]. Meanwhile it has been shown that preliminary exhaustion of the catecholamine reserves leads to depression of metabolism and to a corresponding decrease in heat production in response to cooling. This, in turn, had a beneficial effect on the production of long-term stable hypothermia, to which the name artificial hypobiosis has been given [11].


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