PRINCIPLES GOVERNING DISTURBANCE OF ENERGY METABOLISM IN ACUTE ISCHEMIA OF THE TRANSPLANTED SMALL INTESTINE

L. M. Saburova, N. I. Mosin, and V. A. Bukov

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The reversibility of changes in the glycogen, lactate, and adenine nucleotide level was compared with functional and morphological disturbances accompanying acute ischemia of the transplanted small intestine. The stability of the mucous membrane of the small intestine is maintained under these conditions chiefly by metabolic changes. After restoration of the blood flow circulatory and nervous mechanisms acquire an important role in this process. The transition to an unstable state begins at a critical level of metabolism which is observed, in the case of the mucous membrane of the small intestine, between the first and second hours of acute ischemia.

Progress in transplantation of the small intestine is largely determined by the reversibility of the pathochemical changes developing in the period of acute ischemia, the duration of which may vary considerably. Acute ischemia of the small intestine, even if not exceeding 1 h in duration, can be reflected in its functional state [2, 3].

No information on the reversibility of disturbances in energy metabolism in the mucous membrane of the small intestine of dogs after simulation of acute ischemia and transplantation by various methods could be found in the accessible literature.

The investigation described below was carried out for this purpose.

EXPERIMENTAL METHOD

In experiments on 32 mongrel dogs of both sexes weighing 15-20 kg a segment of the small intestine was isolated for 15-30 min or 1, 2, or 3 h at a temperature of 18-22°C. The graft was then placed in a special constant-temperature chamber and connected to the femoral vessels of an intact dog for 4-6 h. In some experiments acute ischemia was created in situ by clamping the cranial mesenteric vessels for 1 h and subsequently restoring the blood flow. Observations lasted up to 24 h. The concentrations of lactate, ATP, ADP, AMP [5], and glycogen [4] were determined in the mucous membrane of the small intestine before and after restoration of the blood flow. The functional state of the small intestine was estimated from the glucose concentration in the venous blood flowing from the graft after introduction of 10% glucose solution into the lumen of the bowel. The state of the vascular system was studied by contrast angiography and by impregnation by Kupriyanov's method. The numerical results were subjected to statistical analysis [1].

EXPERIMENTAL RESULTS AND DISCUSSION

Catabolic changes in acute ischemia of the small intestine lead to a progressive decrease in the glycogen, ATP, and ADP levels or to their total disappearance ($P < 0.05$). A significant rise in lactate and

Laboratory for Transplantation of Organs and Tissues, Academy of Medical Sciences of the USSR, Moscow. Department of Operative Surgery and Topographical Anatomy, P. Lumumba University, Moscow.
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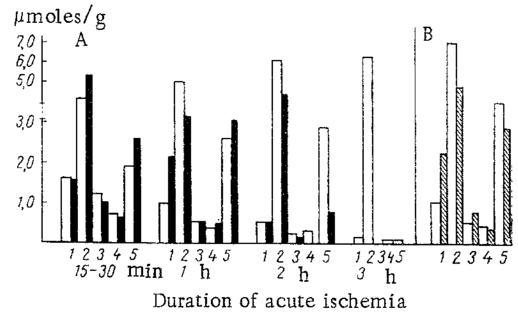

Fig. 1. Concentrations of adenine nucleotides, glycogen, and lactate in the mucous membrane of the small intestine in acute ischemia. A) Acute ischemia of grafts; B) compression of mesenteric vessels in situ for 1 h. 1) Glycogen; 2) lactate; 3) ATP; 4) ADP ($\times 10^{-1}$); 5) AMP ($\times 10^{-2}$). Unshaded columns – before restoration of blood flow; black columns – after restoration of blood flow; obliquely shaded columns – 24 h after restoration of blood flow. Abscissa, duration of acute ischemia; ordinate, concentration of adenine nucleotides, glycogen, and lactate.

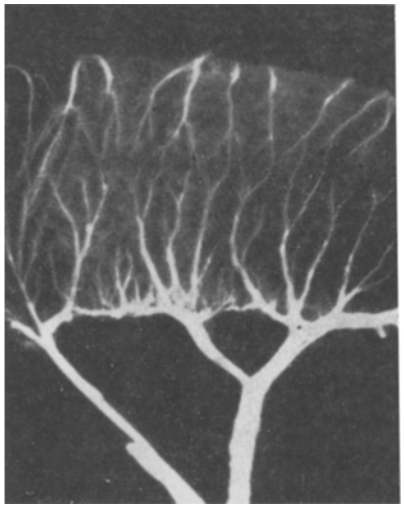

Fig. 2. Angiogram. Transplanted small intestine, ischemia for 20 min; extramural vessels dilated, shape of peripheral arcades modified, intramural vascular system not substantially changed.

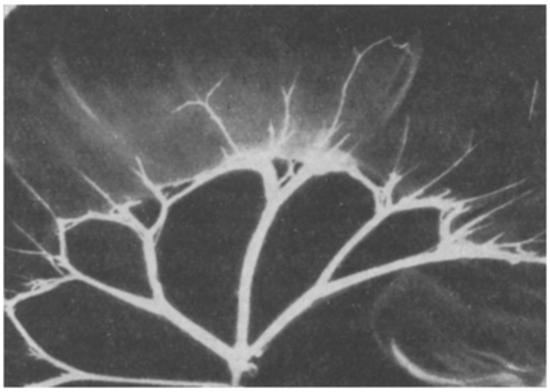

Fig. 3. Angiogram. Transplanted small intestine, ischemia for 2 h: complete occlusion of the intramural vascular system of the intestine.

AMP was observed before 2 h of acute ischemia ($P < 0.05$). After 2 h the rate of rise of the lactate concentration became much slower and the AMP concentration began to fall. The intensity of these processes varied with an increase in the duration of ischemia. The most marked fall of the glycogen and ATP concentrations was observed during the first hour of acute ischemia. Three levels of energy metabolism could be distinguished in acute ischemia. In the first intensive utilization of preformed ATP was combined with intensive glycolytic generation of ATP, maintaining the integrity of the organ. The intensity of utilization of the preformed ATP then fell although the high rate of its glycolytic generation continued. Finally, the rate of both processes slowed down considerably. Because of the variability of the individual parameters it was possible to estimate the level of energy metabolism only by studying all methods together (Fig. 1).

Restoration of the blood flow made it possible to verify the state of the system by functional loading. Glucose absorption was undisturbed by ischemia uner 20 min in duration. The intensity of absorption then decreased or ceased altogether after ischemia for 2 h.

Morphological investigation showed that local disturbances of the hemodynamics connected with the state of the vascular system play an important role in the pathogenesis of the functional disturbances. For example, after ischemia under 30 min in duration the vascular pattern of the perfused intestine was saturated, all the extramural and intramural vessels were filled, and their outlines were smooth, but isolated extravasations of blood appeared and disturbances developed in the system of vertical anastomoses of the vasa recta. The veins were slightly dilated and evidence of stasis appeared in the postcapillaries, venules, and veins (Figs. 2 and 3). With an increase in the duration of ischemia extravasations appeared along the course of the main mesenteric vessels, the peripheral arcades were spontaneously occluded and the vasa recta cut off. If the duration of ischemia exceeded 2 h, the wall of the organ was practically deprived of its blood supply – the blood flow was limited to arterio-venous shunts on the mesenteric border of the intestine.

The primary disturbances of metabolism arising during prolonged acute ischemia and the circulatory disturbances developing later evidently could not be overcome by restoration of the blood flow. After shorter periods of ischemia (under 1 h) a basis for restoration of normal energy metabolism in the intestine still remained.

In a segment of small intestine isolated from the circulation for 1 h by compression of the mesenteric vessels, a tendency toward reversibility of the pathochemical changes and restoration of functional integrity were found as early as 24 h after restoration of the blood flow. The severity of the morphological changes under these circumstances did not differ greatly from that observed in the isolated graft after ischemia for 30-40 min and during the first hours after restoration of the blood flow, despite edema of the organ.

The integrity of the organ during acute ischemia is thus maintained chiefly by metabolic changes. After restoration of the blood flow circulatory and nervous mechanisms evidently play an important role in this process. The transition to an unstable state begins when metabolism reaches the critical level, which for the mucous membrane of the small intestine is observed in the period between the 1st and 2nd hour of acute ischemia.

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