SOME PRINCIPLES GOVERNING TISSUE RESPONSES TO ACUTE ISCHEMIA

L. M. Saburova and L. P. Selivanova

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The glycogen content was investigated before and after restoration of the blood flow in the ischemic kidney, small intestine, and limb. After ischemia lasting 2 h for the kidney and 1 h for the small intestine, the glycogen level at the end of perfusion was higher than the intravital level. The absorption spectrum of iodine complexes of glycogen under these conditions was similar to normal for the small intestine, but not typical for glycogen for the kidney.

KEY WORDS: ischemia; glycogen; perfusion of isolated organs.

Investigation of metabolic disturbances in organs before transplantation has led to the formulation of the concept of the critical level of metabolism; for the striated muscles of the limb this arises between 3 and 6 h of acute ischemia, in the renal cortex after 2 h, and in the mucous membrane of the small intestine between 1 and 2 h of acute ischemia at room temperature [1, 2, 4, 5].

With an increase in the duration of acute ischemia, the glycogen content in tissues falls or may disappear completely. Recovery of the circulation in the ischemic organs is accompanied by accumulation of glycogen, sometimes to above the intravital level.

A qualitative and quantitative study of glycogen was therefore carried out during acute ischemia of various tissues.

EXPERIMENTAL METHOD

Striated muscles from a limb (36 experiments), the renal cortex (37 experiments), and the small intestine (25 experiments), taken from mongrel dogs of both sexes (14-25 kg) were subjected to acute ischemia for periods of 1-24 h at room temperature. The circulation in the ischemic organ was restored by the extracorporeal route by transfusing with blood from a recipient dog or by perfusion with the AIK RP-64 artificial circulation apparatus for 3-6 h. The surgical part of the experiments was carried out by T. M. Oksman, V. A. Bukov, and M. V. Bilenko. For a control, tissues exposed to "minimal" ischemia for 10-15 min, the period necessary for restoration of the blood flow in the ischemic organ, were used. In all the experiments glycogen was isolated by alkaline extraction and this was followed by enzymic determination of glucose [3]. The structure of glycogen in the mucous membrane of the small intestine and the renal cortex was studied by Krisman's modification [7] of Stepanenko's method [6]. To photograph the absorption spectrum in the region from 325 to 700 nm, 2.6 ml of a solution consisting of KI-I_2 and 5.55 M $CaCl_2$ was added.

EXPERIMENTAL RESULTS AND DISCUSSION

The ability of the ischemic tissues to restore the normal glycogen content depended on the period of ischemia. Restoration of the blood flow in the tissues after a minimal period of ischemia did not always lead to complete normalization of the glycogen level (Fig. 1). At periods of ischemia measuring 6 h for

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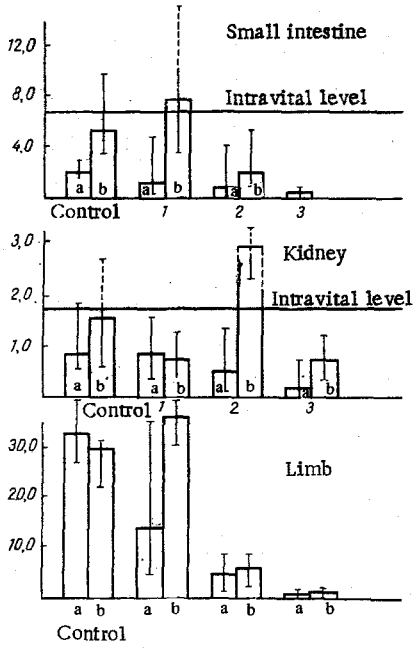

Fig. 1. Glycogen concentration in tissues after acute ischemia: a) before, b) after restoration of blood flow. Vertical lines show limits of variation of the parameter. Abscissa, period of ischemia (in h); ordinate, glycogen level (in μmoles/g).

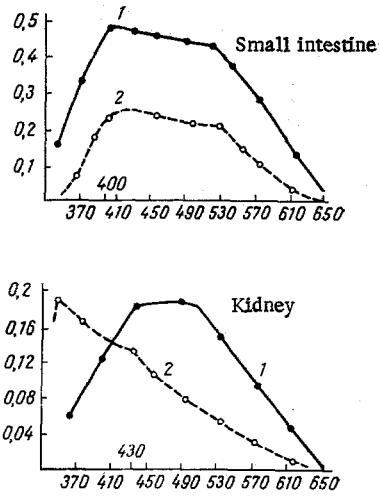

Fig. 2. Absorption spectrum of iodine complexes of glycogens isolated from mucous membrane of small intestine and renal cortex of dogs before (1) and after (2) restoration of blood flow. Abscissa, wavelength (in nm); ordinate, absorption (in units).

muscle tissue, 3 h for the kidney, and 2 h for the small intestine, ability to restore the normal glycogen concentration was virtually lost. The intermediate periods of acute ischemia behaved somewhat specially: 3 h for muscle tissue, 2 h for the kidney, and 1 h for the small intestine. After restoration of the blood flow at these periods of ischemia an increase in the glycogen content in the tissue was observed to a level much higher than the intravital level. This rule was most evident in the renal cortex and the intestinal mucosa, for which glycogen is not the principal form of energy accumulation. In muscle tissue, in which glycogen is the principal source of energy for mechanical work, excessive accumulation of glycogen was observed in only 2 of 36 cases.

The study of iodine complexes with glycogen isolated from the mucous membrane of the ischemic intestine showed that their absorption maximum occurred at 400 nm, compared with 430 nm for glycogen from the renal cortex under the same conditions (Fig. 2). After restoration of the blood flow in the small intestine the peak of glycogen absorption and the character of the curve remained unchanged. Meanwhile the substance isolated under these conditions from the renal cortex gave an absorption spectrum atypical for glycogen. Evidently this was a high-molecular-weight polymer of glucose that was isolated from the tissue by alkaline extraction and gave the characteristic complex with KI-I_2 for such compounds.

The low intravital glycogen concentration in the kidney and small intestine makes it difficult for these tissues to compensate for their energy deficit by glycolysis. Presumably restoration of the blood flow in these tissues not only restores some aspects of their metabolism to normal, but also leads to the uncoordinated biosynthesis of glycogen or of some other glucose polymer that can be used for the glycolytic generation of energy should a further oxygen deficiency arise.

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