TABLE 2. Results of Morphometry of Lysosomal Structures of Mouse Liver Cells (in % of total volume of lysosomal structures in "fraction")

Fraction	Radius of structures, μ	Hepatocytes				Sinusoidal cells				Total volume of secondary lysosomes in fraction
		1	2	3	Total 1, 2, 3	1	2	3	Total 1, 2, 3	
N	1,920—0,490	—	—	11,7	11,7	25,1	16,9	46,3	88,3	74,9
M	0,470—0,254	8,2	49,1	—	57,3	33,4	9,3	—	42,7	58,4
L	0,235—0,192	32,5	40,6	6,3	79,4	12,5	8,1	—	20,6	55,0
MS	0,166—0,096	43,1	27,8	1,2	72,1	24,1	3,8	—	27,9	32,8

Legend. 1) Primary lysosomes, 2) secondary lysosomes of auto- and heterophagous type, early stage, 3) secondary lysosomes of auto- and heterophagus type, late stage. N) Nuclear fraction, M) mitochondrial fraction, L) lysosomal fraction, MS) microsomal fraction.

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LIPID PEROXIDATION IN THE GRAFT AND RECIPIENT'S TISSUES UNDER DIFFERENT CONDITIONS OF TRANSPLANTATION

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When tissues such as glands of internal secretion, skin and, in particular, large whole organs are transplanted, a lasting clinical effect, in the shape of true survival of autografts, or lengthening of primary survival of homografts, is observed only if they retain their viability. In tissues with no circulation and also in isolated tissues surviving *in vitro*, incompletely oxidized products of glycolysis and ions of metals of variable valency accumulate, changes take place in the composition and structure of phospholipids, and the antioxidative activity of lipids is reduced, all of which may contribute to an increase in the intensity of lipid peroxidation (LPO) [1, 2, 4, 5, 7, 11, 12]. Accumulation of endogenuous products of LPO has been shown to lead to marked inhibition of functional activity of isolated tissues, thus indicating the important role of the intensity of LPO in viability [6].

During transplantation tissues again find themselves under unfavorable conditions — until their circulation is restored they are in an ischemic state. In addition, the graft sur-

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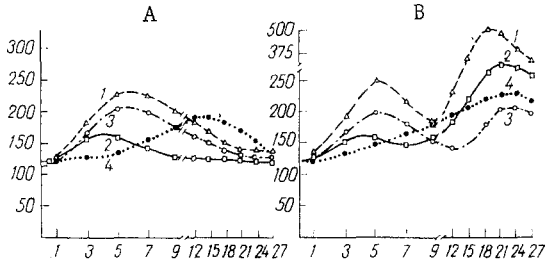

Fig. 1. Changes in intensity of CL of skin at different times after autografting (A) and homografting (B). 1) Graft; 2) graft after two injections of α-tocopherol (80 mg/kg); 3) graft after two injections of immunodepressant; 4) recipient's skin adjacent to graft. Abscissa, time (in days); ordinate, intensity of CL (in counts/10 sec).

vives under conditions of immunologic incompatibility. It is evident that until the graft had taken, disturbances of its structure may be reflected in changes in the intensity of LPO. However, the kinetic principles of LPO during grafting by different methods have been inadequately studied. Yet it can be postulated on the basis of the writers' previous investigations [2, 3] and the results of other research [9, 10] that an increase in the intensity of LPO and the structural and functional disturbances caused by its products in membranes of graft cells may be one of the factors causing rejection of the graft.

The object of this investigation was to study changes in the intensity of LPO in a graft and in the recipient's tissues at various stages of auto- and homotransplantation.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 3.0-3.5 kg. Autologous and homologous skin was transplanted in the form of a full-thickness skin graft measuring 3 × 4 cm. Changes in the intensity of LOP in the graft, in the recipients' tissue adjacent to the graft and in the recipient's blood were investigated 1-27 days after transplantation. Six rabbits were used at each time point. With the different methods of transplantation, the intensity of LPO of the skin graft was judged from changes in the intensity of chemiluminescence (CL) and in the concentration of malonic dialdehyde (MDA), and its intensity in the recipient's blood was judged from changes in the MDA concentration. The intensity of CL of the skin grafts was recorded on a photometric system utilizing the FEU-85 instrument, the principles of which were described previously [3, 8]. The MDA concentration was determined by the method described in [3]. In some experiments the action of antioxidants and immunodepressants on the intensity of LPO in the grafts was studied. The antioxidant α-tocopherol was injected intramuscularly twice (from the 3rd and 9th days of the experiment) in doses of 80 mg/kg. Immunodepressants (prednisolone + cortisone) were injected intramuscularly in a dose of 110 mg/kg. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

After transplantation the intensity of LPO in the grafts and the other tissues tested showed considerable changes. The intensity of CL in the autografts began to rise 24 h after transplantation, and continued to do so for 5 days, but after the 6th day, when connections between the graft and the recipient's tissues were restored, the intensity of CL in the autografts fell steadily for the next 21 days of the experiments, when they had reached the normal level of intact skin (120 counts/10 sec). After this period and until the end of the experiment there were no appreciable changes in the intensity of CL of the skin autografts (Fig. 1A). The same rule was characteristic of MDA in the autografts after transplantation as for CL — a marked increase in its concentration during the first 5 days after grafting, then a fall until the 18th day, after which MDA was maintained at a constant level (Fig. 1B).

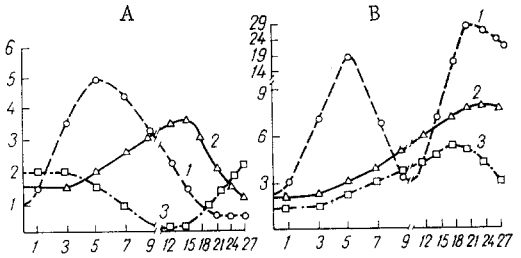

Fig. 2. Changes in MDA concentration in skin tissue and blood at different times after autografting (A) and homografting (B). 1) Skin graft; 2) recipient's skin adjacent to graft; 3) recipient's blood. Abscissa, time (in days); ordinate, MDA concentration (in nmoles MDA/mg protein).

After autografting changes in the intensity of LPO also occurred in the skin adjacent to the graft. For instance, from the 3rd-5th days after transplantation the intensity of CL and the MDA concentration increased in samples of skin adjacent to the autograft. The intensity of LPO in the recipient's skin continued to increase until the 12th-14th days after transplantation, but after that time values of LPO in the recipient's skin adjacent to the graft gradually returned to its initial levels (Fig. 1A, B). Changes in the MDA concentration were found in the recipient's blood also after autografting. The MDA concentration in the blood of rabbits undergoing autografting fell after the 3rd day of the experiment, and by the 9th day after transplantation it was below the normal level. Not until the 21st day after transplantation was the blood MDA concentration restored to the control level (Fig. 1B).

Experiments showed that the kinetics of the intensity of CL in the homografts during the first 9 days after transplantation was similar to that observed in autografts: an increase in the intensity of CL in the grafts during the first 5 days followed by a small decrease until the 9th day after transplantation. However, by contrast with autografting, the intensity of CL in homografts increased stadily from the 9th day of the experiment, to reach a second maximum 18-21 days after transplantation, when its intensity was 4 times its initial value (Fig. 2A). After reaching a maximum the intensity of CL then fell appreciably, evidently because of exhaustion of the phospholipid substrate in the grafts. The same rule was found in the changes in MDA concentration in the homografts as for CL: an increase during the first 5 days up to a 1st maximum, followed by a 2nd maximum 18 days later (Fig. 2B). During homografting, a continuous rise in the intensity of CL and in the MDA concentration was observed starting from the 3rd day of the experiment until the 21st day in the recipients' skin adjacent to the graft and in the recipients' blood, by contrast with what was found during autografting, after which the intensity of LPO in these recipients' tissues declined (Fig. 2).

The study of the mechanisms of the increase in intensity of LPO after transplantation showed that administration of antioxidants (α-tocopherol) to the recipients appreciably lowered the intensity of the first maximum of LPO in both autograft and homograft (Figs. 1A and 2A). However, administration of antioxidants had no significant effect on the change in the second maximum of LPO in the homograft (Fig. 2A). Injection of immunodepressants into the recipient, however, although not changing the height of the first maximum of LPO, appreciably reduced the height of the second maximum, and shifted it toward the later periods of the experiments (Figs. 1A and 2A). These facts suggest that the sudden increase in the intensity of LPO in the second half of the experiment in the homograft was due to immunologic injury. Considering regulation of LPO by antioxidants during the first 5 days of the experiment, and also the weakening of LPO in the grafts after morphological contact had been established with the recpient's tissue, it can be concluded that the first maximum of LPO was linked with a disturbance of metabolism in the surviving graft under ischemic conditions in the early period after transplantation, as a result of which the endogenous antioxidants were quickly used up.

Analysis of these experimental data thus shows that a change in the intensity of LPO, characterizing the level of oxidative free-radical processes in the graft, in the recipient's tissues adjacent to the graft, and in the recipient's blood depends on the type of transplantation and correlates with the functional state of the graft at all stages of its survival.

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EFFECT OF ANOXIA UNDER DIFFERENT CONDITIONS ON KINETICS OF LIPID PEROXIDATION IN CELL ORGANELLES

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Facts indicating that anoxia is the main cause leading to intensification of lipid peroxidation (LPO) in cells of isolated tissue have recently accumulated. During survival after death, products of LPO accumulate in isolated organs and tissues and antioxidative activity is reduced [2-4, 6]. Inhibition of the functional activity of isolated tissues also have been demonstrated during induced lipid peroxidation, i.e., in the presence of an increased concentration of LPO products [5].

LPO products are known to be capable of causing an increase in the membrane permeability of organelles, the release of enzymes from them, inactivation or transformation of enzymes, oxidation of thiols, and polymerization of proteins; for that reason the intensification of LOP during postmortem survival may aggravate damage to the cell membranes of isolated tissues [1, 9]. Meanwhile, free-radical injury to the whole membrane system of the cells of isolated surviving tissues has not been adequately studied. There have been few investigations primarily aimed at studying changes in the intensity of LPO in organelles exposed to ischemia in tissues [4].

During ischemia in the tissues, because of different velocities of LPO in different organelles, the possibility of diffusion of LPO products from some areas of the cell to others

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