created were an inadequate stimulus for manifestation of all the histogenetic potentials of these cell forms. There is strong experimental evidence in support of this latter suggestion. It has been shown that connective tissue from different sources can create the conditions for development of the epidermis [5], for the repeated organization of derivatives, even from predetermined cells in perinatal mammals, specific interaction with the fibroblasts of the dermis is necessary [7, 8]. This interaction is responsible for the type of derivatives formed in embryogenesis, and for their arrangement [4]. The deeper layers of the skin are without such an influence [6].

The model suggested in this paper can be effectively used in future research aimed at studying these problems.

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EFFECT OF ANTIBODIES TO LYSOSOMAL ENZYMES ON COURSE OF EXPERIMENTAL BURN SHOCK

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In burn shock, marked disturbances of the microcirculation develop as a result of disorders of the systemic circulation [7, 9]. Changes in the nutritive blood flow lead to tissue hypoxia and acidosis, which lead to disturbances of the integrity of the lysosomal membrane and release of lysosomal hydrolases into the intercellular space and systemic blood flow [3, 4]. Lysosomal enzymes circulating in the blood stream during burn shock maintain and aggravate existing disturbances of the hemodynamics; in our experiments with artificially raised blood enzyme levels, injection of lysosomal enzymes into healthy animals caused inhibition of cardiac muscle activity and disorders of the microcirculation [4]. Substances inactivating lysosomal enzymes in the blood in burn shock include not only Trasylol (aprotinin) and its derivatives, but also specific antibodies to the soluble fraction of lysosomes. In experimental

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TABLE 1. Cathepsin D Activity, Hematocrit Number, and Parameters of Oxygen Balance and Acid–Base State of Blood of Healthy and Burned Rats, Receiving Isotonic Saline with Immunoglobulins (M ± m)

Parameter	Series of experiments			
	I	II	III	IV
	healthy rats	burned rats		
		untreated	IS and globulins of nonimmune rabbits	IS and antienzyme immunoglobulins
	10	12	10	10
Cathepsin D activity, nmoles tyrosine·min^{-1}·ml plasma^{-1}	0,2±0,06	0,76±0,1*	0,85±0,22	0,3±0,05***
H, liter/liter	0,49±0,01	0,55±0,01*	0,55±0,01	0,52±0,01***
Hb, g/liter	16,0±0,6	21,9±0,7*	22,0±0,4	18,5±0,5***
$p\bar{v}O_2$, mm Hg	41,3±2,1	29,7±2,3*	34,8±1,1	39,4±0,8***
$Hb_{\bar{v}}O_2$, %	60,4±4,8	31,3±5,4*	37,6±6,2	56,7±3,6***
pH, units	7,263±0,03	7,105±0,02*	7,075±0,03	7,190±0,02***
BE, mmoles/liter	−8,9±0,07	−19,3±1,7*	−18,9±0,9	−11,4±0,9***
HCO_3	17,8±0,7	11,1±1,4*	11,6±0,5	16,9±1,0***
pCO_2 mm Hg	41,4±4,7	37,0±4,4*	42,2±2,0**	40,0±3,1***

Legend. Significance of differences ($p > 0.05$): *) Between results of series I and II, **) series II and III, ***) series III and IV.

hemorrhagic shock the use of antiserum to lysosomal hydrolases [10, 11] increase the length of survival of the animals.

In the investigation described below the effect of antienzyme antibodies on the course of burn shock is studied.

EXPERIMENTAL METHOD

Altogether 4 series of experiments were carried out on 91 male and female albino rats: series I) healthy animals, series II) untreated burns. A standard burn of the IIIA-IIIB degree affecting 13-15% of the body surface was inflicted under open ether anesthesia, by means of a light and heat generator [6]. In the experiments of series III, 30 min after thermal trauma the rats were given an intraperitoneal injection of isotonic saline solution (IS: 15 ml/kg) and globulins of an unimmunized rabbit; the experiments of series IV differed from those of series III in that, besides the crystalloid solution, the animals were given an injection of antienzyme immunoglobulins. Blood samples were taken 3 h after trauma from the internal jugular vein. The animals were then killed with an overdose of thiopental sodium. No blood samples were taken from some of the animals in each of the groups II, III, and IV. In these experiments, the survival rate of the animals was determined in the course of 24 h. Activity of lysosomal cathepsin D [13], the protein concentration [12], and hematocrit number (H) were determined in the blood. The concentration of hemoglobin (Hb) and the degree of its saturation with oxygen (Hb_vO_2), the partial pressure of oxygen (p_vO_2), and parameters of the acid–base state of the blood were recorded on the ABL-2 instrument ("Radiometer," Denmark). Immunoglobulins were obtained from the serum of rabbits after immunization with soluble fraction of lysosomal enzymes [8], isolated from rat liver. Globulins were isolated from the immune and normal sera by affinity chromatography on a column, where protein A – agarose was used as the immunosorbent [5]. The dose of the immunoglobulins for injection into the rats was calculated on the basis of the results of titration of the immunoglobulins; it was 4 mg/100 g body weight. Serum globulins from unimmunized rabbits were injected in the same dose. The results were analyzed by nonparametric statistical tests [2].

EXPERIMENTAL RESULTS

After thermal trauma (series II) cathepsin D activity in the animals' blood increased: it was three times higher than in intact rats of series I (Table 1). Hemoconcentration developed, as could be judged from the increase in the hematocrit number and hemoglobin concentration per unit volume of blood. Oxygenation of the venous blood is reduced: the partial pressure of oxygen and the oxygen saturation of the blood decreased, evidence of the develop-

ment of hypoxia. Marked metabolic acidosis was observed: pH and the partial pressure of CO_2 in the blood decreased, and the buffer base deficit rose sharply. All 19 rats left for determination of their length of survival died in the course of 24 h, 13 of them during the first 7 h after trauma (68%).

After injection of the globulin fraction of an unimmunized rabbit with IS (series III) the parameters recorded were virtually the same as those in the animals of series II. Of the 13 rats of this series, 3 (23%) died during the first 7 h after trauma, whereas 30% of the animals survived longer than 24 h.

Different results were obtained after injection of immunoglobulin fraction to lysosomal enzymes with IS (series IV). Cathepsin D activity in the animals of this series was close to normal (Table 1). The hematocrit number and blood hemoglobin concentration were significantly lower than in rats of series II and III. All this is evidence of reduction of the hemoconcentration. The hypoxia and also the metabolic acidosis were significantly less marked, judging by oxygenation of the venous blood. Of 17 rats none died during the first 7 h. Survival more than 24 h was recorded for 41% of animals.

Injection of the immunoglobulin fraction to lysosomal enzymes with IS in burn shock thus caused the cathepsin D activity in the blood to fall. Improvement of oxygenation of the venous blood observed in these experiments can be explained by restoration of the circulation, due to weakening of the cardiodepressive action of the lysosomal enzymes [1]. As a result of restoration of the oxygen supply to the tissues, tissue metabolism improved, as shown by correction of the acidosis after injection of the antienzyme immunoglobulins.

The use of antibodies to lysosomal enzymes as a component of infusion therapy in burn shock led to an increase in the length of survival of the animals.

Thus specific inhibition of lysosomal enzymes leads to correction of various functions of the body, disturbed as a result of thermal trauma, confirming the important role of lysosomal enzymes in the pathogenesis of shock. The use of the immunoglobulin fraction to lysosomal enzymes may be one way of making the treatment of shock more effective.

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