behavioral changes in animals and shifts of sensitivity to pain accompanying them after the end of long-term exposure to stress.

These experiments thus showed that long-term immobilization of rats gives rise to lasting nonopioidergic hypoalgesia, which continues throughout the period of immobilization and is unconnected with hunger and thirst of the animals. After the termination of immobilization this hypoalgesia quickly disappears. The repeated use of the opiate antagonist naloxone throughout the period of immobilization leads to spontaneous aggressiveness of the animals and reliable hypoalgesia when it ends.

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COOLING THE VASCULAR BED OF AN ORGAN MAKES ANOXIA A LESS EFFECTIVE STIMULUS

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KEY WORDS: hypothermia; anoxia; skeletal muscle; small intestine; arteries and veins.

In publications devoted to the study of the effect of oxygen deficiency in the blood and of acute hypothermia on the arteries [3, 7] and veins [15] of organs and on their filtration–absorption ratios [4, 6, 10, 11, 13], no information can be found on the combined action of these two factors. The study of this problem is of great theoretical and practical importance for the characterization of the joint functions of peripheral vessels. This has become possible thanks to the development of new techniques whereby the parameters of the resistive, capacitive, and metabolic functions of the vascular bed of an organ can be recorded simultaneously [8].

The aim of this investigation was to compare the magnitude and direction of changes in the macro- and microhemodynamics in skeletal muscle and the small intestine during exposure to the separate and combined action of cooled blood and an anoxic stimulus on the vascular bed.

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TABLE 1. Background Values of Parameters of Macro- and Microhemodynamics in Muscle and Intestine

Experimental conditions	Organ	Parameter			
		R_a, mm Hg/100	R_V, g/(ml·min)	P_c, mm Hg	CFC, ml·100 g/min·mm Hg
Normothermia, normoxia					
Before action of anoxic stimulus	Muscle	22,8±1,96	0,84±0,12	14,7±0,5	0,040±0,003
	Intestine	2,90±0,23	0,38±0,035	18,3±0,7	0,090±0,005
Before action of cooled blood	Muscle	21,5±1,70	0,86±0,12	14,5±0,4	0,043±0,003
	Intestine	2,96±0,23	0,39±0,035	18,5±0,7	0,095±0,004
Hypothermia of blood, normoxia					
Before action of anoxic stimulus	Muscle	26,1±1,80	1,05±0,12	15,8±0,5	0,062±0,006
	Intestine	3,85±0,25	0,48±0,035	21,8±0,8	0,062±0,004

EXPERIMENTAL METHOD

Experiments were carried out on 24 male and female cats weighing 2.5-4 kg, anesthetized with urethane and chloralose (1 and 0.01 g/kg respectively), with the use of heparin (1500 U/kg). The gastrocnemius muscle or the small intestine was isolated from the circulation, leaving its nervous connections with the rest of the body intact. The vascular bed of these two regions was perfused with the animal's own blood by means of a constant-output pump [5]. The pressure in the popliteal vein was set at 10 mm Hg [5] and in the intestinal vein at 6 mm Hg [4]. The pre- and postcapillary resistance (R_a and R_V respectively), the mean capillary pressure (P_c), and the capillary filtration coefficient (CFC) were recorded by the method in [8]. In each experiment the parameters of the macro- and microhemodynamics were determined successively under the influence of an anoxic stimulus (10% O_2 in nitrogen), with the animal breathing naturally, under normothermic conditions (37 ± 0.5°C), then during local cooling of these vascular regions, achieved by lowering the temperature of the blood entering the organ to 30 ± 0.2°C and, finally, vascular effects were studied during the combined action of cooled blood (30 ± 0.2°C) and anoxia 10 min after the beginning of inhalation of the respiratory mixture. The assigned temperature of the blood entering the organ was maintained by means of a heat exchanger and ultrathermostat (V 15c, East Germany). The animal's body temperature (measured in the esophagus) and the temperature of blood in the organ were recorded by means of transducers of the TPÉM-1 type. The parameters were recorded on an automatic writer of the N-327-8 type. The results were subjected to statistical analysis by the Fisher–Student's test.

EXPERIMENTAL RESULTS

Data relating to changes in the parameters of vascular function in the muscle and intestine under the influence of the stimuli chosen for investigation are expressed as percentages of their initial (background) values. The background values in absolute terms are given in Table 1.

The degree and character of changes in the parameters of vascular function in the two organs taking place as a result of making the animals breathe an anoxic mixture for 10 min are shown in Figs. 1 and 2 (unshaded columns). The action of the anoxic stimulus lowered R_a and increased CFC by more than 30% in both vascular beds. This last parameter, reflecting a change in area of the metabolic vessels and their permeability, is considered [9] to depend on the tone of the "precapillary sphincters," which, through dilatation induced by the action of the oxygen deficiency in the blood, evidently led to an increase in area of the microvascular surface, unless there was a simultaneous and considerable increase invascular permeability [1]. Under these circumstances P_c increased in the muscle (Fig. 1) and decreased in the intestine (Fig. 2), evidently as a result of differences in response of the organs to venous hypoxia. There was a corresponding increase in R_V in the muscle and a decrease in this parameter in the intestine. It can be postulated on this basis that the anoxic stimulus, applied during normothermia of the body as a whole and of the organs, induced constriction of the veins in the muscle and dilatation of the veins in the intestine, leading to corresponding changes of capillary pressure in the organs. Dependence of this parameter of the microhemodynamics on venous tone, at least during perfusion of the vascular bed under continuous blood flow conditions, has been proved theoretically [8] and experimentally [2].

Hypothermia of the organs also caused considerable changes in the parameters characterizing resistive (R_a and R_V) and metabolic (P_c and CFC) functions of the vascular bed (Figs.

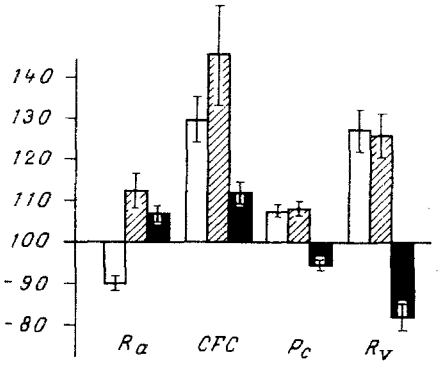

Fig. 1

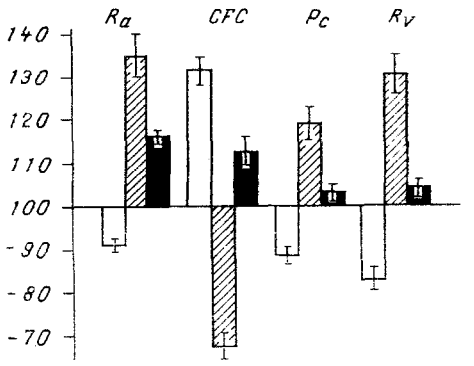

Fig. 2

Fig. 1. Changes in R_a, R_v, CFC, and P_c during separate and combined exposures of vessels of a skeletal muscle to cooled blood and to an anoxic stimulus (in percent of initial level). Here and in Fig. 2: unshaded columns — during anoxia; obliquely shaded columns — combination of hypothermia and anoxia; vertical lines — mean error of mean ± m_x.

Fig. 2. Changes in R_a, R_v, P_c, and CFC during exposure of vessels of small intestine to cooled blood and anoxic stimulus separately and together. Legend as to Fig. 1.

1 and 2, obliquely shaded columns). By contrast with this, CFC in the intestine fell by 30%, against the background of an increase in the remaining parameters of vascular function of this organ (Fig. 2). Differences between the organs with respect to the degree and direction of the changes in parameters of vascular function, observed in the present investigation, are in agreement with data in the literature [12].

Thus exposure to anoxic and hypothermic stimuli separately caused statistically significant ($p < 0.05$) changes in the parameters of the vascular function in all cases described (Figs. 1 and 2). The direction and degree of these changes depended both on the stimulus presented and on the organ to which the vascular bed belonged.

An anoxic stimulus of the same intensity as in the first case (normothermia of the body as a whole and of blood entering the organ), against the background of cooling of the organ, induced a much smaller deviation of parameters of the macro- and microhemodynamics, which was manifested particularly clearly on the intestinal vessels, where deviations of P_c and R_v from their initial levels were not statistically significant ($p > 0.05$). It must be noted that the deviations observed in the vessels of both organs reversed their sign (see Figs. 1 and 2, black columns). Changes in the action of anoxia against the background of cooling also were observed in relation to R_a, and under these conditions this parameter was increased in both vascular beds; hence it can be concluded that anoxia, under the conditions described, led not to dilatation, but to constriction of the arteries of the muscle and intestine. Whereas the anoxic stimulus under normothermic conditions increased CFC in the muscle by 30% of its initial level, during cooling of the organ it did so by only 12%. In this case, a possible explanation of this phenomenon is that the initial level of CFC in the cooled muscle was already 50% above its initial level during normothermia (Fig. 1). However, in the intestinal vessels this parameter was lowered as a result of cooling of the organ by more than 30% of its initial value during normothermia, and presentation of the anoxic stimulus against this background, like in the experiments on muscle, caused an increase of 12% in CFC above its initial level which, in the long run, was one-third of the deviation of CFC when anoxia was applied against the background of normothermia of the body as a whole and of the intestine (Fig. 2).

These results are evidence that local cooling of the blood vessels causes them to be desensitized with respect to an anoxic stimulus, as was observed in the experiments on both organs, and which applied to a greater or lesser degree to all the parameters of vascular function tested. The effect of desensitization of the vascular bed of the organ under these circumstances was very difficult to explain, for in some cases the sign of the deviation of the parameter during selective (i.e., without background cooling) exposure of the animal and, correspondingly, of the vascular bed of the organ, to anoxia was reversed. In light of this,

the view that cooling leads to inhibition of metabolic processes in the tissue and to a decrease in their oxygen consumption (and for that reason the anoxic stimulus is less important) [14] is oversimplified and requires analysis and detailed scrutiny.

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EFFECT OF VITAMIN E AND THYMALIN ON THE DEVELOPMENT OF EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS

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It was reported previously that during the development of experimental allergic encephalomyelitis (EAE) lipid peroxidation (LPO) is activated in the blood and brain of animals immunized with an encephalitogenic emulsion [9]. At the same time it has been shown that there is a marked deficiency of the T-lymphocyte population and their functional activity is depressed in EAE and multiple sclerosis [3, 5, 11, 12, 14].

In this investigation, to establish the pathogenetic role of intensification of LPO in EAE, an attempt was made to reproduce the neuroallergic process in noninbred albino rats, which are resistant to EAE, against the background of avitaminosis E, i.e., when the antioxidant balance in the body is disturbed, and to demonstrate whether it is possible to correct the pathological process by acting on the T-cell stage of immunity. For this purpose, in experiments on guinea pigs, which are sensitive to EAE, immunization with encephalitogenic material was carried out after administration of vitamin E and the polypeptide thymus preparation — thymalin. There is evidence in the literature that the number of T suppressor cells

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