zones. Potentiation of the alimentary hypercholestermia was found, as was also observed by other workers during stimulation of all zones of the hypothalamus, together with a rise in the arterial pressure. The latter effect may probably be due to changes in the reactivity of the morphologically and functionally changed blood vessels to neurogenic stimulation, with a tendency toward the appearance of constrictor effects [11].

The results provide an explanation for clinical observations which show that even positive emotions may give rise to attacks of angina or may lead to myocardial infarction in patients with coronary atherosclerosis [5, 7].

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ROLE OF THE LUNGS IN REGULATION OF ACTIVITY OF THE KALLIKREIN – KININ SYSTEM IN IMMOBILIZATION STRESS

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Activation of the kallikrein–kinin system (KKS) in various pathophysiological situations is primarily compensatory in its role, regulating the state of the blood, the microcirculation, and the hemodynamics as a whole. The dynamics and degree of participation of kinins in these processes are determined by the ratio between activating (Hageman factor, kallikrein, etc.) or regulating (inhibitors, kininases) biochemical components of the system.

An important role in this regulation is played by the microcirculatory system of the lungs, the endothelium of which possesses powerful kinin-destroying activity [7]. Protease inhibitors with a marked anti-kallikrein action also have been isolated from the lungs. It is logical to suggest that not only factors limiting the effectiveness of the kinin system, but also those with the opposite effect, promoting it, may be localized in the pulmonary microvessels. This suggestion is more likely to be correct because the lungs are known

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TABLE 1. Dynamics of KKS Indices for Arterial and Venous Blood of Rats during Immobilization Stress (M ± m)

Blood	Index	Control (n = 7)	Immobilization		
			1 h (n=7)	3 h (n=6)	24 h (n=8)
Venous	SEA	3,5±1,9	4,8±1,8	8,2±2,7*	2,2±2,0
	PK	63,1±6,7	30,8±4,6*	39,1±8,8*	31,9±3,7*
	KI	1,64±0,10	1,68±0,15	1,51±0,13	1,60±0,28
Arterial	SEA	1,8±0,7	0,5±0,2 †	4,3±2,0	0,6±0,2
	PK	6,02±4,8	63,9±13,0 †	48,1±6,5	35,2±4,3*
	KI	1,87±0,05 †	1,74±0,09	1,84±0,05	1,82±0,04

Legend. PK and SEA levels given in μmoles hydrolyzed BAEE/h/ml plasma, KI in relative units; n) number of experiments; *P < 0.05 relative to control; †P < 0.05 for arteriovenous difference.

to be connected with synthesis or inactivation of many physiologically active substances concerned in the regulation of the blood and circulatory systems [3, 8, 11]. In particular, the presence of kininase, with antidepressor enzyme activity, in the lungs is combined with the function of the angiotensin-converting pressor system.

There were two main aims of the investigation to be described: to study changes in activity of the KKS in the course of immobilization stress and to compare the state of the KKS in blood samples taken "before the lungs" and "after the lungs" in the course of immobilization stress.

EXPERIMENTAL METHOD

Noninbred male rats weighing 250-300 g were used. Immobilization stress was induced by fixing the unanesthetized animals in the supine position for 1, 3, and 24 h. The animals were anesthetized with pentobarbital (5 mg/100 g), after which blood was taken simultaneously from the right and left ventricles by direct puncture after thoracotomy with artificial ventilation. Indices of the KKS, including spontaneous plasma orginine esterase activity (SEA), the prekallikrein concentration (PC), and the total kallikrein inhibitor (KI) were determined in blood plasma by Colman's method [10] in the writers' modification with N-α-benzoyl-L-arginine ethyl ester (BAEE, from Reanal, Hungary) as substrate, and using 2-hydrazono-2,3-dihydro-3-methylbenzothiazole (from Serva, West Germany) in the final stage of determination of enzyme activity [5].

EXPERIMENTAL RESULTS

The results given in Table 1 show that there was virtually no difference between the SEA values and PC level in the control animals for venous and arterial blood. The KI level was a little higher in arterial blood. After immobilization for 1 h changes indicating marked activation of the KKS in venous blood were observed. The PC concentration was reduced by more than half and SEA was increased. These changes, it will be noted, were completely absent in arterial blood. In blood which had passed through the lungs the PC level was equal to its initial value and the arteriovenous difference for SEA also was significant ($P < 0.05$). After immobilization for 3 h SEA in venous blood was even higher, the PC remained low as before, and a tendency was noted for the KI level to fall. These changes point to continued and increasing activation of the kinin system. Arterial blood levels after immobilization for 3 h again differed from those in venous blood: The SEA level was lower but the PK and KI concentrations were a little higher. However, at this stage the difference was much less marked and the arteriovenous difference was no longer significant, i.e., activation of the kinin system due to immobilization stress had now spread to the arterial system. After immobilization for 24 h activation of the KKS was expressed equally in venous and arterial blood.

These results direct attention to the following essential points. Immobilization stress induces acute and considerable hemodynamic and microcirculatory changes in the animal. During immobilization of rabbbits a marked rise of arterial pressure was found 15 min after the beginning of the procedure, and it continued for 2 h [13]. Immobilization of rats for 5-6 h caused the arterial pressure to change in different directions [6]. As early as 1 h after the beginning of immobilization, aggregates of erythrocytes formed in the mesentery of the rats, "plasmatic" blood vessels appeared, arteriolo-venular shunts opened, and the blood flow in the venules was slowed, with the development of prestasis and stasis and also of disturbances of vascular permeability for ink particles [4]. These disturbances intensified as the period of immobilization lengthened. Immobilization of rats for 24 h increased the sensitivity of the terminal arterioles to adrenalin and noradrenalin [12]. These changes in the hemodynamics and microcirculatory system were bound to affect the kinin system – one

of the most important systems of hemovascular regulation in the body. Immobilization stress was accompanied by a fall in the blood kininogen level in rats [9]. The present experiments showed that the kinin system responds by rapid activation, which is already pronounced after immobilization for 1 h. A characteristic feature is the difference between the indices for the kinin system in arterial and venous blood, reported here for the first time, which indicates that in the acute stage of stress PK leaves the lungs, to compensate for its high consumption in the venous circulation. An important role is also played by the pulmonary arginine esterase inhibitor, on account of which the SEA level in the arterial blood falls again. In the first stages of immobolization stress, systems responsible for kinin formation thus operate intensively both at the periphery and in the lungs, i.e., at this stage the KKS performs an undoubted adaptive function.

The compensatory response of the lungs relative to the KKS revealed during continued immobilization stress was less marked, although traces of it were still apparent after 3 h. Under the conditions of this pathophysiological model the adaptive role of the lungs was perhaps essential but temporary in character.

The lungs also probably play a role in the regulation of KKS activity in other pathological or physiological situations. In experimental myocardial infarction the writers previously [2] observed restoration of the "labile" kininogen level in blood which had passed through the lungs. Valeev et al. [1] found an arteriovenous difference for PK, SEA, and KI values in patients with craniocerebral trauma. In the present writers' opinion this difference may be related to the compensatory role of pulmonary systems.

It can thus be concluded from these data that the lungs play an important role in regulating the functional state of the blood KKS through their action in localizing and liberating factors which both "trigger" and limit the activity of that system.

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