The results are evidence that the inhibitory action of stress factors extends both to the endocrine activity of the testes and to the gonadotrophic function of the pituitary. As our previous studies showed [2], preliminary stimulation of pituitary gonadotrophic function by exogenous LH RH does not prevent depression of the endocrine activity of the testes during stress. These data, and also the dissociation observed in this investigation in the course of LH and testosterone in the poststress period, suggest that LH deficiency does not play a pathogenetic role in the disturbance of secretory activity of the testes during stress. The inhibitory effect of stress factors is aimed simultaneously at the pituitary and gonads, with the maximal disturbance at the level of the testes.

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EFFECT OF THE THYMUS ON IMMUNOREACTIVE PEPTIDE ACTIVITY

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UDC 612.438:612.018:612.017.1

KEY WORDS: thymus, thymectomy; thymalin; cytomedins; peptides.

A new class of mediators of intercellular interaction, known as cytomedins, in the biocontrol system of multicellular organisms has recently been isolated and described. These substances are polypeptides of basic nature and they are responsible for intergenic interactions in populations of specialized cells [6]. We know that the cytomedins from different organs contain peptides capable of influencing differentiation of immunocompetent cells and of interacting with the system for hemostasis and fibrinolysis [2]. However, the role of these compounds in the mechanism of protective reactions of the whole organism is not yet clear. Meanwhile thymectomy, when carried out in particular in the early stages, inhibits immunity and causes hypercoagulation and depression of fibrinolysis [1]. The impression is created that regulatory factors of peripheral organs cannot interact in the absence of the thymus. Experiments described below were undertaken to test this hypothesis.

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(Presented by Academician of the Academy of Medical Sciences of the USSR N. V. Vasil'ev.) Translated from Byulleten' Éksperimental'noi Biologii Meditsiny, Vol. 107, No. 2, pp. 234-236, February, 1989. Original article submitted February 19, 1988.

0007-4888/89/0002-0252$12.50

TABLE 1. Effect of Polypeptides on Parameters of Immunity

Parameter	Animals undergoing mock operations and receiving physiological saline (n = 10)	Animals after thymectomy, receiving polypeptides from organs of rats undergoing thymectomy (T) and mock operation (MO)								
		control (physiological saline; n=10)	peptides from muscle		control (physiological saline; n=10)	peptides from liver		control (physiological saline; n=10)	peptides from spleen	
			T (n=10)	MO (n=10)		T (n=10)	MO (n=10)		T (n=10)	MO (n=10)
Number of T lymphocytes in peripheral blood per 100 cells of mononuclear fraction	50,86±1,28	34,2±2	37,8±1,8	43,13*±1,6**	37,4±1,57	36,1±1,05	49,3*±1,5**	32,87±0,68	34,29±0,74	42,75*±1,28**
Number of B lymphocytes in peripheral blood per 100 cells of mononuclear fraction	37,93±1,27	28±0,99	27,43±1,41	33,75*±1,18**	27±1,0	28,83±1,09	36,73*±1,23**	37,46±0,73	28,86±0,6	36,46*±0,5**
Hemagglutinin titer	7,07±0,195	5,06±0,4	5,33±0,23	6,13*±0,16**	5,4±0,15	5,8±0,02	7*±0,209**	5,4±0,13	5,6±0,19	7,06*±0,24**
Hemolysin titer	7,14±0,17	6,2±0,17	6,46±0,133	6,93*±0,18**	6,1±0,23	6,3*±0,26	7,21*±0,214**	5,86±0,16	6,06±0,15	7,33±0,185**
Number of AFC per 10^6 splenic karyocytes	71,15±1,64	60,46±1,69	61,14±1,19	69,2*±1,94**	57±2,15	60,58±1,2	70,64*±1,58**	56,5±2,52	57,75±2,41	71,08*±1,64**

Legend. Here and in Table 2: *$p \leq 0.05$ between peptides from organs of MO animals and control; **$p \leq 0.05$ between peptides from organs of MO rats and animals after T.

TABLE 2. Effect of Polypeptides on Parameters of Thromboelastogram and Fibrinolysis

Parameter	Animals undergoing mock operations and receiving physiological saline (n = 10)	Animals after thymectomy, receiving polypeptides from organs of rats undergoing thymectomy (T) and mock operation (MO)								
		control (physiological saline; n=10)	peptides from muscle		control (physiological saline; n=10)	peptides from liver		control (physiological saline; n=10)	peptides from spleen	
			T (n=10)	MO (n=10)		T (n=10)	MO (n=10)		T (n=10)	MO (n=10)
R	2,87±0,16	1,7±0,095	2,0±0,26	2,3±0,44**	1,9±0,054	1,9±0,054	2,75±0*,18**	1,83±0,06	1,58±0,073	2,0±0*,066**
K	1,51±0,1	0,92±0,07	0,7±0,44	1,22*±0,081**	0,6±0,031	0,58±0,026	1,42±0*,14**	0,81±0,04	0,69±0,048	1,72*±0,098**
R + K	4,39±0,17	2,6±0,11	2,71±0,24	3,6±0,1**	2,6±0,11	2,56±0,064	4,28±0,19	2,6±0,074	2,27±0,1	3,9±0,11
t	4,85±0,18	4,0±0,067	4,1±0,08	4,0±0,1*	3,6±0,18	3,8±0,23	3,5±0,21	4,52±0,1	4,27±0,14	4,62±0*,11**
M. A.	3,39±0,18	5,2±0,21	4,28±0,33	4,5±0,14*	4,46±0,079	3,8±0,08	5,04±0*,11**	5,22±0,17	2,33±0,098	5,36±0,026
α	15,7±0,75	20,7±1,1	19,4±0,75	15,5±0,77*	26,5±1,2	25,6±0,57	16,1±0,78	24,±0,88	29,2±0,92	19,2±0,99
i	1,27	0,39	0,34	0,7	0,31	0,29	1,11	0,32	0,25	0,74
Fibrinolysis of euglobulins	256,25±6,49	323±4,2	317,8±3,47	280,6±3*,99**	308,5±5,86	302,1±4,02	268±5*,38**	326,5±5,18	321,9±5,15	255,8±5*,94**
of kaolins	34,05±1,42	46,6±1,8	46,5±1,52	30,25±1*,2**	40,1±1,55	47±2,1	26,35*±0,95**	47,3±1,78	56,4±2,05	32,9±1,2**

EXPERIMENTAL METHOD

Experiments were carried out on 90 rats after thymectomy and 10 rats after mock operations. Three months after the operation the animals were divided into three groups, which were given an intramuscular injection of 1 mg/ng (sic) of polypeptide factors from the liver spleen, and muscles of rats after thymectomy and the mock operation, obtained by the method of Morozov and Khavinson [5], 5 days before immunization and 5 days thereafter, once daily. Rats after thymectomy and the mock operation, which received physiological saline by the same scheme, served as the control. The rats were immunized by a single intraperitoneal injection of a suspension of washed sheep's red blood cells (SRBC) in physiological saline in a final concentration of $1 \cdot 10^7$. The animals were killed 5 years (sic) after immunization and titers of hemolysins and hemagglutinins [8] and the number of T and B lymphocytes in their blood were determined. The number of AFC [4] per 10^6 karyocytes was counted in the animals' spleen. To determine immunocompetent peripheral blood cells, monospecific antisera were obtained against rat thymocytes [12] and immunoglobulins (Ig) of the G class [11], and absorbed. Next, IgG was isolated from them by ion-exchange chromatography [13] and it was fixed with the aid of glutaraldehyde on previously trypsinized SRBC [10]. Ultimately cells loaded with antibodies to rat IgG were used to determine B lymphocytes, and cells loaded with antibodies to thymocytes were used to determine T lymphocytes. The results of the reaction were read as the number of T-RFC and of B-RFC per 100 cells of the mononuclear fraction, isolated from peripheral blood on a Ficoll–Urotrast density gradient [7]. The state of the hemostasis system was judged by parameters of thromboelastography and the fibrin clot lysis time [3].

EXPERIMENTAL RESULTS

The experiments showed that thymectomy, performed in the first month after birth, leads to reduction of the number of immunocompetent peripheral blood cells and is the cause of the low titer of homolysins and hemagglutinins and of reduction of the number of AFC in response to primary immunization by SRBC (Table 1), and it also leads to the development of hypercoagulation and of depression of fibrinolysis (Table 2). Changes arising after thymectomy were not suppressed by correction following subsequent injection of peptides from the organs of thymectomized rats. Depression of immunity, hypercoagulation, and inhibition of fibrinolysis persisted in the animals (Tables 1 and 2), whereas in response to injection of peptide fractions from the organs of animals undergoing mock operations, stimulation of the immune response, an increase in the number of T and B lymphocytes, lengthening of parameters of the thromboelastogram, and activation of fibrinolysis were observed. Under these circumstances, restoration of the system for immunogenesis and hemostasis corresponded to the level of the same parameters in animals undergoing a mock operation and receiving physiological saline (Tables 1 and 2).

The fact will be noted that peptide factors form the spleen and liver of rats undergoing mock operations virtually did not differ from one another in their action on immunity, hemostasis, and fibrinolysis, whereas peptides from muscle were appreciably less active. Meanwhile each of the peptide factors possessed much greater ability to exert their influence on immunity than on hemostasis. The existence of an immune mechanism controlling the hemostasis system was reported previously. Polypeptides from organs of animals undergoing mock, operations, by normalizing the parameters of immunity of rats after thymectomy, probably thereby ensure recovery of the immunologic component of regulation of the hemostasis system; peptides from organs of animals undergoing thymectomy do not possess this ability.

Analysis of the data suggests that the role of cytomedins is not limited to regulation of gene activity in a population of specialized cells. These molecules evidently play the role of information messengers. During interaction with circulating lymphocytes, the signals transmitted by them enable lymphocytes, on the one hand, to form an integral idea of the events taking place in the population of functioning cells, and on the other hand, they ensure the optimal level of their differentiation and activity, essential for an adequate response to the information obtained. The fact that peptide complexes from organs of thymectomized animals did not possess this ability suggests that production of T lymphocytes is by no means the only function of the thymus. Synthesis of mediators of intercellular interaction (cytomedins) in peripheral organs and tissues is evidently controlled through the system of hormones synthesized by this gland. Probably on this basis it is easy to explain the fact that the polypeptide factor of the thymus, namely thymalin [9], when used therapeutically in the majority of pathological processes, gives a positive effect, leading to restoration of the original cytomedin levels in different organs. This is why we consider it useful to give thymalin together with cytomedins, synthesis of which is disturbed in the affected organ.

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