function of hetero-organic antigens is as follows: like other factors of the thymus they have an influence on differentiation of the various subpopulations of its lymphocytes, including the T_μ and T_γ cells of the organ.

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EFFECT OF POLYPEPTIDES FROM THE THYMUS, BONE MARROW, AND BURSA OF FABRICIUS ON IMMUNOGENESIS AND HEMOSTASIS IN NEONATALLY THYMECOTIMIZED AND ANTENATALLY BURSECTOMIZED CHICKENS

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Polypeptide factors from the thymus (thymosin, thymalin, etc.), bone marrow (antibody producer stimulator, hemalin, etc.), and bursa of Fabricus (bursilin) are known to act on different stages of lymphocyte differentiation [4, 6, 8, 9]. Thymalin has been shown to activate differentiation of T lymphocyte precursors selectively into mature T cells and also to correct disturbances of immunity and hemostasis in thymectomized rats [6, 10]. Injection of polypeptide factors from the bursa of Fabricius into neonatally bursectomized chickens normalizes the immune response to T-dependent and T-independent antigens and abolishes disturbances in the regulation of hemostasis [4]. Experiments on mice, rats, and guinea pigs have shown that hemalin stimulates the formation of B lymphocytes and increases their number in the circulation, in the thymus, and in the spleen of thymectomized animals, and also stimulates proliferative processes in the bone marrow [7].

Neonatal thymectomy in birds leads to selective blocking of differentiation of T lymphocytes and to disturbances of cell-mediated immunity [13], whereas bursectomy in ovo is accompanied by profound changes in humoral immunity, which are much more marked than those after neonatal bursectomy [12].

Considering that the state of immunity of an organism is reflected in the course of its hemostatic responses [3] it was decided to assess the level of immunity, hemostasis, and fi-

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brinolysis in bursectomized and thymectomized birds receiving polypeptides from the thymus, bone marrow, and bursa of Fabricius.

EXPERIMENTAL METHOD

Experiments were carried out on 120 chickens. During the first 6 h after birth thymectomy was performed on 45 birds, and bursectomy was performed on 60 chickens at the 18th-19th day of embryonic development. The remaining chickens, which constituted the control group, underwent mock operations at these same times. After the operation the birds were given injections of 10 mg chloramphenicol for 7 days. The room in which the chickens were kept was irradiated with a bactericidal lamp. The experiments began 1.5 months later. Immunodeficient birds were injected intramuscularly with polypeptides from the bursa of Fabricius, bone marrow, or thymus (1 mg/kg body weight in each case) for 1 week. All preparations were obtained by the method of Morozov and Khavinson [5] and were polypeptides of basic nature with mol. wt. of 2 to 10 kilodaltons.

Immunity in the chickens was assessed with respect to the following parametes: the titer of hemagglutinins and hemolysins, the number of antibody-forming cells (AFC) in response to immunization with sheep red blood cells. AFC were determined by the method in [11]. The birds were immunized by a single intravenous injection of sheep red blood cells in a dose of $70 \cdot 10^9$ cells/kg body weight and the above-mentioned tests were carried out 6 days later.

The state of hemostasis was assessed with respect to the following parameters: the blood clotting time, plasma recalcification time, kaolin, prothrombin, and thrombin times, fibrinogen concentration, and degree of euglobulin lysis [1].

The numerical results were subjected to statistical analysis with calculation of the index of significance (p).

EXPERIMENTAL RESULTS

The immune response to injection of xenogeneic red blood cells was depressed in the immunodeficient birds, especially in the bursectomized chickens (Table 1). Meanwhile, hy-

TABLE 1. State of Immunity in Chickens (M ± m)

Parameter studied	Intact chickens (n = 15)	Bursectomy (n = 12)				Thymectomy (n = 12)		
		physiological saline	bursilin	hemalin	thymalin	physiological saline	bursilin	hemalin
Hemagglutinin level, $\log_2$	5,7±0,5	0,8±0,3*	3,2±0,4**	1,9±0,2**	1,9±0,4	2,4±0,2*	4,5±0,4**	2,8±0,5
Hemolysin titer, $\log_2$	3,8±0,4	1,4±0,3*	3,4±0,3**	1,1±0,4	2,1±0,3	1,9±0,2*	3,6±0,6**	1,7±0,2
AFC after immunization (× 10^3)	14,4±0,8	5,2±0,6*	10,9±1,1**	6,3±0,9	6,7±1,0	10,1±0,9*	16,2±0,8**	11,4±0,7
Leukocytes (10^9/liter)	28,3±1,3	22,2±1,2*	27,2±1,4**	23,1±1,2	26,3±0,9**	22,6±0,9*	25,6±0,8	24,7±1,3

Legend. *) Differences between intact and immunodeficient chickens receiving physiological saline are significant; **The same, between immunodeficient birds receiving physiological saline and chickens receiving polypeptide factors. n) Number of birds.

TABLE 2. State of Hemostasis in Chickens (M ± m)

Paramter studied	Intact chickens (n = 14)	Bursectomy (n = 12)				Thymectomy (n = 12)		
		physiological saline	bursilin	hemalin	thymalin	physiological saline	bursilin	hemalin
Blood clotting time, sec	554±21	404±16*	488±19**	437±21	432±24	497±0*	580±12**	514±11
Recalcification time, sec	392±16	281±16*	331±18	301±10	286±19	354±8	393±7**	365±10
Kaolin time, sec	277±10	221±13*	254±15	236±10	219±13	237±5*	270±6**	251±7
Prothrombin time sec	135±9	89±8*	132±12**	112±6	94±5	109±5*	134±4**	129±6
Thrombin time, sec	33,3±1,3	24,8±1,7*	28,9±1,1	25,1±1,2	26,2±0,8	26,1±0,8*	28,8±0,9	29,1±1,2
Fibrinogen, g/liter	11,3±0,6	23,2±2,1*	11,8±1,2**	13,9±1,1**	18,9±1,8	21,3±1,5*	12,3±0,7**	19,6±1,3
Fibrinolysis, min	236±14	337±20*	264±14**	258±10**	295±18	229±9	227±12	236±21

percoagulation, a raised fibrinogen level, and inhibition of fibrinolysis were observed in these birds (Table 2).

After injection of bursilin into the bursectomized chickens normalization of the parameters of immunity and blood clotting was observed. The hemagglutinin titer rose in bursectomized birds receiving hemalin, the fibrinogen concentration fell, and fibrinolysis was accelerated. Injection of thymalin into these birds caused an increase in the number of leukocytes in the peripheral blood. Parametes of hemostasis and immunity were fully restored to normal in thymectomized chickens receiving bursilin, but injection of hemalin had no effect on the state of these systems.

The very weak action of hemalin on thymectomized and bursectomized chickens can perhaps be explained on the grounds that only the early stages of development of lymphocytes take place in the bone marrow, i.e., the formation of precursors of T and B cells [2, 12], and for that reason polypeptides from the bone marrow have no effect on the later stages of lymphoid cell differentiation. The weaker restoration of immunity and hemostasis by bursilin in chickens after bursectomy in ovo compared with neonatal bursectomy is due to the fact that after the latter operation some cells are able to pass through differentiation in the thymus and bursa and to migrate into peripheral lymphoid organs. Under these circumstances only quantitative changes were found in the composition of the lymphocytes. Removal of the bursa of Fabricius on the 18th day of embryonic development led to more qualitative changes in lymphocyte differentiation [12]. Hence it can be postulated that additional microenvironmental factors are required for the development of B lymphocytes in the bursa.

Normalization of the state of the hemostasis system in immunodeficient birds by means of immunoregulatory peptides is due to restoration of the physiological immune mechanism of regulation of blood clotting and fibrinolysis [3, 10].

The data given above are evidence of the important role of polypeptide factors of the bursa of Fabricius in the regulation not only of humoral, but also of cell-radiated immunity.

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