kemoid reaction syndrome in mice with hemangiopericytoma, in the writers' opinion, is a convenient experimental model with which to study and identify factors capable of influencing the number of stem cells and maturation of monocytes and granulocytes. Besides its purely theoretical interest, the isolation of such factors could be of practical interest, for they could be used to influence the regeneration of hematopoietic tissue when damaged in the course of cytostatic therapy. The writers have suggested that factors of humoral nature are responsible for the development of the leukemoid reaction in mice with tumors. Delmonte [6] succeeded in isolating from a transplantable mammary gland carcinoma a humoral factor capable of inducing proliferation of stem cells and discharge of leukocytes into circulation. However, the etiological role of other agents and, in particular, of viruses, which are frequent "passengers" of transplantable tumors, cannot be ruled out.

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IMMUNOLOGIC REACTIVITY AND ADRENOCORTICAL FUNCTION IN THE EARLY PERIOD OF CHEMICAL CARCINOGENESIS

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A parallel study was made of the level of immunologic reactivity and the state of adrenocortical function in BALB/c mice 7 days after a single injection of various doses of methylcholanthrene. Definite correlation was found between the degree of immunodepression induced by different doses of methylcholanthrene and determined as the number of antibody-forming cells in the spleen of the experimental mice and the 11-hydroxycorticosteroid concentration (both free and bound) in the blood plasma of the mice 7 days after injection of the carcinogen. These results may indicate that adrenocortical hormones play an important role in the pathogenesis of immunodepression induced by a chemical carcinogen.

KEY WORDS: carcinogenesis; immunodepression; antibody-forming cells; 11-hydroxycorticosteroids.

Immunodepression is an important pathogenetic stage in the formation and progression of the neoplastic process and it accompanies the development of the neoplasm from the moment of generation of the transformed cell until death of the host as a result of the formed tumor.

The mechanism of development of immunodepression due to the presence of a tumor differs from that of immunodepression associated with the induction of a tumor by chemical carcinogens or irradiation. In the

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TABLE 1. Effect of Immunization with Test Antigen on Plasma 11-HCS Level in BALB/c Mice (M ± m)

Group of animals	Number of animals	11-HCS concentration, mg %		
		bound	free	total
Control intact mice	9	16,7±1,3	1,9±0,5	18,4±1,6
Experimental mice receiving following injections over a period of 4 days:				
0.5 ml physiological saline intraperitoneally	6	18,2±0,5	1,8±0,3 $P>0,05$	20,0±0,3
$5 \cdot 10^8$ Sheep's erythrocytes intraperitoneally	18	15.0±1,0	3,8±0,7 $P<0,05$	18,8±1,5
$5 \cdot 10^8$ Sheep's erythrocytes intravenously	6	13,7±2,8	4,0±0,6 $P<0,05$	17,5±3,1

TABLE 2. Number of Antibody-Forming Cells in Spleen and Plasma 11-HCS Level in BALB/c Mice 7 Days after Single Injection of Various Doses of MC (M ± m)

Group of animals	Dose of MC, mg	Number of animals	Number of 19S AFC (per million nucleated cells in spleen)	11-HCS concentration, mg %					
				without immunization			after immunization		
				bound	free	total	bound	free	total
Control (intact)	—	9	—	16,7±1,3	1,9±0,45	18,4±1,6	—	—	—
Immunized with test antigen	—	18	336,6±27,09	—	—	—	15,0±1,0	3,8±0,7	18,8±1,5
Receiving carcinogen	0,2	18	188,1±8,03	19,7±1,5	5,3±1,4	25,7±1,2	21,9±4,1	10,6±0,3	32,5±0,4
	0,5	18	176,0±8,48	46,3±0,4	21,6±1,5	67,9±5,2	25,2±0,8	6,9±0,8	34,4±3,0
	1	18	138,0±6,28	40,7±2,9	17,4±1,6	58,1±4,3	14,2±0,7	5,1±0,5	19,3±0,9
	1,5	18	93,5±3,14	31,4±7,0	14,2±1,4	45,7±11,1	20,1±1,2	5,6±0,4	25,8±1,5
	2	18	97,1±7,34	26,4±2,5	8,5±0,9	34,9±10,0	14,9±0,9	6,7±0,9	21,5±1,8

first case the cause of the immunodepression may be particular substances such as the nuclear factor from Ehrlich's ascites tumor [1, 12], RNA from the tumor cells [2], and so on. During induction of a tumor by chemical carcinogens, irradiation, or viruses immunodepression develops indirectly, in the writers' view by a change in the state of adrenocortical function.

The object of the present investigation was to study correlation between the indices of immunologic reactivity and the functional state of the adrenal cortex in mice with immunodepression induced by a chemical carcinogen.

EXPERIMENTAL METHOD

Experiments were carried out on 130 male BALB/c mice aged 1.5-2 months. Immunologic reactivity was studied by determining the number of antibody-forming cells (AFC) in the spleen of the experimental mice 4 days after intraperitoneal injection of a test antigen ($5 \cdot 10^8$ sheep's erythrocytes) by the local hemolysis in gel method [11]. This index, as several workers have found [3, 6, 8, 13, 14], objectively reflect the degree of immunodepression.

Immunodepression was induced by means of the chemical carcinogen 20-methylcholanthrene (MC), which was injected intramuscularly into the experimental mice in doses of 0.2, 0.5, 1, 1.5, and 2 mg in 0.1 ml apricot oil. The number of AFC in the spleen and the plasma concentration of free, protein-bound, and total 11-hydroxycorticosteroids (11-HCS), which reflect the state of adrenocortical function most objectively [5, 7], were determined in the mice 7 days later.

The 11-HCS concentration was determined fluometrically [10] and free and bound 11-HCS were separated by gel-filtration on fine-grain Sephadex G-50.

The data were subjected to statistical analysis and the coefficient of correlation was determined between individual groups of experimental results.

EXPERIMENTAL RESULTS

Since the degree of immunodepression was tested after intraperitoneal injection of the test antigen, a preliminary study was made to discover if injection of the antigen itself changes the plasma 11-HCS level in BALB/c mice. The results are given in Table 1, and their analysis shows that in response to injection of the test antigen the concentration of free 11-HCS in the blood plasma, i.e., the active fraction playing an important role in the realization of the response of the body to any form of stimulation [4, 9], was doubled.

Simultaneous testing of the degree of immunodepression and plasma 11-HCS level in BALB/c mice was next carried out 7 days after a single injection of different doses of MC. The results are given in Table 2 and show that the degree of immunodepression, estimated as the number of AFC in the spleen of the mice, depends to a definite degree on the dose of carcinogen injected. Injection of 0.2 mg MC into the mice reduced the number of AFC in the spleen after 7 days by 44%, whereas the maximal dose (2 mg MC) reduced it by 72%, i.e., the higher the dose of carcinogen, the deeper the state of immunodepression.

Injection of MC led at the same time to an increase in the plasma 11-HCS concentration, both free and protein-bound. Injection of MC in a dose of 0.2 mg increased the concentration of the most active (free) 11-HCS by 2.8 times ($P < 0.05$), in a dose of 0.5 mg by more than 11 times, but in a dose of 1 mg by 9 times. These results indicate definite correlation between the dose of the carcinogen and the plasma 11-HCS concentration. A further increase in the dose of MC led to a smaller increase in the 11-HCS concentration, probably because of maximal strain on adrenocortical function [5].

The study of the plasma 11-HCS concentration in mice immunized intraperitoneally with sheep's erythrocytes 7 days after injection of various doses of MC showed a marked increase in the level of free and protein-bound 11-HCS in the mice receiving the carcinogen in a dose of 0.2 mg, compared with these indices in unimmunized animals (5.8 times higher than in intact animals and 2.8 times higher than in immunized animals). Meanwhile, the 11-HCS concentration fell appreciably in mice receiving the larger doses of MC. These results, in the writers' opinion, are evidence that two stimulating factors, such as high doses of MC and the test-antigen, by their interference lead to overstrain followed by depression of adrenocortical function.

However, it must be pointed out that the free 11-HCS level in both the immunized and unimmunized mice, receiving different doses of the carcinogen, was significantly higher than in the intact animals and also the immunized mice not receiving the carcinogen.

Injection of MC thus leads to the development of immunodepression and a connected increase in the level of adrenocortical hormones (especially of free 11-HCS) in the blood plasma of mice 7 days after a single injection of various doses of the carcinogen. Considering the important role of free 11-HCS in the mechanism of the response to the specific components of the stimulus, the high glucocorticoid level in the recipients can be presumed to be one of the factors leading to the development of immunodepression under the influence of MC.

In the writers' opinion these data can be regarded as evidence that adrenocortical hormones play an important role in the genesis of immunodepression induced by a chemical carcinogen.

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THERMOSENSITIVITY OF SPECIFIC TRANSPLANTATION ANTIGENS OF THE TUMOR CELL MEMBRANE

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A study of tumor specific transplantation antigen (TSTA) on the cell membrane of SV40-induced tumors and spontaneous hepatomas of inbred Syrian hamsters and also of monkey cells infected in vitro with tsA-mutants of SV40 virus demonstrated its high temperature sensitivity. Heating the cells to 56°C for 30-60 min led to the total loss of their immunogenic activity. Moreover, in animals immunized by tumor cells heated to 56°C, stimulation of growth of the test tumor cells was regularly observed.

KEY WORDS: tumors; transplantation antigens; immunogenicity; thermosensitivity.

Inactivation of tumor cells by heating followed by their use for experimental purposes for specific immunization against tumors has been a frequently used method of action on tumors. The loss of the immunogenic properties of tumor cells during the use of this method, as also of certain other physical or chemical methods of treatment of tumor cells (lyophilization, extraction, glutaraldehyde treatment) has been observed

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