Comparison of the results suggests that only immune mouse lymphocytes, on contact with syngeneic red cells, can secrete the suppressor factor which probably participates in the regulation of the immune response. Secretion of suppressor factors observed on contact between immune lymphocytes and cells of the same genotypes may play a role in the maintenance of the normal function of the T and B systems of immunity. A disturbance of this mechanism may perhaps play a role in the development of autoimmune diseases.

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IMMUNOCOMPETENCE OF LYMPHOCYTES FROM PREGNANT MICE STUDIED IN GRAFT VERSUS HOST REACTION

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The ability of lymphocytes taken during the second trimester from C57BL/6 mice mated with CBA males to induce the graft versus host reaction in (CBA × C57BL/6)F_1 hybrids was weaker than that of cells both of virgin donors and of mice pregnant after syngeneic mating. This was reflected in lengthening of the life span of the experimental recipients and weakening of inhibition of endogenous colony formation in the spleen of sublethally irradiated hybrids. This ability was restored at the end of pregnancy and in some experiments it actually exceeded the control.

KEY WORDS: *graft versus host reaction; pregnancy.*

There is no question about the important role of the mother's cellular immunity in preventing immunological conflict with her own fetus [1, 2, 5]. One of the main manifestations of the immunological activity of lymphocytes is their ability to induce a graft versus host reaction (GVHR). The writers are aware of only a few investigations in which this test was used to study cellular immunity in pregnancy. With the local GVHR as model, a nonspecific lowering of immunological reactivity has been demonstrated in the second half of pregnancy incompatible for the H-2 complex, but not syngeneic, in mice [9]. In experiments using systemic and local GVHR, evidence was obtained of an increase in sensitization of maternal lymphocytes to transplantation antigens of paternal origin [8, 10].

In the investigation described below the ability of lymphocytes of the spleen and lymph nodes of the parents to induce a systemic GVHR in their offspring (F_1 hybrids) was studied.

EXPERIMENTAL METHOD

Experiments were carried out on virgin female C57BL/6 mice and (CBA × C57BL/6)F_1 hybrids of both sexes. The mice were obtained from the nursery of inbred animals, Academy of

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TABLE 1. Activity of Lymphocytes of Pregnant Mice in the GVHR

Experiment No.	Pregnant C57BL/6 donors: from ♂ CBA II	from ♂ CBA III	from ♂ C57BL/6 II	from ♂ C57BL/6 III	from ♂ F1 (CBA×C57BL/6) II	from ♂ F1 (CBA×C57BL/6) III	Virgin C57BL/6 donors	Dose of lymphocytes (×10)	Type of cells	Number of recipients	Life span, days	P
1	±	—	—	—	—	—	—	120	sc	7	26,0±2,1	<0,01
							+	120	sc	6	17,0±2,2	
2	+	—	—	—	—	—	—	30	lc	12	20,0±1,4	>0,05
							+	30	lc	12	19,8±1,5	
3	+	—	—	—	—	—	—	150	sc	10	29,9±2,4	<0,01
							+	150	sc	7	22,0±0,7	
4	+	—	—	—	—	—	—	33	lc	8	18,6±0,4	>0,05
							+	33	lc	7	20,8±1,3	
5	—	+	—	—	—	—	—	30	lc	5	15,4±0,7	<0,05
							+	30	lc	12	19,8±1,5	
6*	—	+	—	—	—	—	—	18	lc	8	16,5±1,0	>0,05
							+	18	lc	8	17,1±1,2	
7*	—	+	—	—	—	—	—	18	sc	12	23,8±1,1	>0,05
							+	18	sc	12	22,2±1,7	
8	—	—	—	+	—	—	—	32	lc	10	17,5±0,7	<0,05
							+	32	lc	11	22,3±1,0	
9	—	—	—	—	+	—	—	47	lc + sc	11	22,1±2,5	>0,05
							+	47	lc + sc	10	23,3±1,3	
10	—	—	—	—	+	—	—	30	lc + sc	8	31,4±2,6	>0,05
							+	30	lc + sc	9	25,0±2,8	
11	—	—	—	—	—	+	—	106	sc + lc	11	21,4±1,3	>0,05
							+	106	sc + lc	11	22,9±1,4	

Legend. 1. Asterisk — recipients irradiated in a dose of 500 R. 2. sc) Spleen cells; lc) lymph node cells; II-III) trimesters of pregnancy; lc + sc taken in the ratio 1:1.

TABLE 2. Number of Endogenous Colonies in Spleen of (CBA × C57BL/6) Mice 9 Days after Irradiation in a Dose of 500 R and Transplantation of $8 \cdot 10^6$ Lymph Node Cells of C57BL/6 Mice

Group	Donors of lymphocytes (C57BL/6 mice)	Period of pregnancy, days	Number of recipients	Number of endogenous colonies in spleen (M ± m)	Index of inactivation, %	P_1	P_2
1	—	—	37	11,8±0,9	0±9,4		
2	Virgin	—	52	1,3±0,24	89,0±4,3		
3, a	Mated with ♂ CBA	9—12	34	7,4±0,8	37,3±8,3	<0,001	
3, b	Mated with ♂ C57BL/6	18—21	17	4,3±1,6	63,6±12,0	<0,05	
4, a		9—13	13	3,61±1,2	69,5±13,1	>0,05	<0,05
4, b		18—21	15	3,20±1,1	72,9±11,8	>0,05	>0,05

Legend. P_1) Significance of differences in inactivation index compared with group 2; P_2) ditto compared with group 3a.

Medical Sciences of the USSR (Stolbovaya). The age of the female donors of lymphocytes was 3 months and that of the recipient hybrids was 2-4 months. To obtain a dated pregnancy, C57BL/6, CBA, or (CBA × C57BL/6)F_1 males were kept in cages with females for 2-3 days. The pregnant donor females were killed in the second or third trimester and the weight of the spleen and thymus and, in some experiments, of the para-aortic lymph nodes was determined. A suspension of lymphocytes was prepared from the spleen and lymph nodes of the donors by the method described previously [3]. The suspension was injected into the retro-orbital venous sinus. The GVHR was assessed with respect to the life span of the animals and the degree of inhibition of endogenous colony formation in the spleen of sublethally irradiated recipients [4]. In the latter case and also in experiments Nos. 10 and 11 (Table 1) the recipient hybrids were irradiated 2-4 h before injection of lymphocytes with ^{60}Co γ rays on the "Luch-1" apparatus in a dose of 500 rad. The recipients were killed on the ninth day, their spleens were immersed in Bouin's fixing fluid for 30 min, and the number of colonies in them was then counted macroscopically. Control animals received the same dose of lymphocytes, taken from virgin donors, as the experimental animals.

EXPERIMENTAL RESULTS

As Table 1 shows, in the experiments in which lymphocytes taken in the second trimester of allogeneic pregnancy (experiments Nos. 1-4) were injected a tendency was observed for the

mean life span of the recipients to be longer than in the control. However, the results were significant only in experiments in which splenic lymphocytes were injected (experiments Nos. 1 and 3).

On the other hand, lymph node cells taken from donors in the third trimester of pregnancy possessed increased immunological activity (experiments Nos. 5, 6, and 8). This was manifested in both allogeneic and syngeneic pregnancy. After combined injection of spleen cells and lymph node cells (in the ratio of 1:1) from donors with semiallogeneic pregnancy no significant differences were found in the life span of the experimental and control animals (experiments Nos. 9, 10, and 11).

The results of a quantitative assessment of the ability of cells from pregnant donors to give a GVHR as revealed by the test of inhibition of endogenous colony formation are given in Table 2. The index of inactivation of endogenous colonies in the spleen of sublethally irradiated hybrids after injection of lymph node cells taken during the second and third trimeters of allogeneic pregnancy were considerably lower than after injection of cells from both virgin donors and syngeneically pregnant mice. The degree of inhibition of endogenous column formation by lymphocytes taken from syngeneically pregnant donors was the same as in the control.

In the second trimester splenomegaly was observed and was more marked in allogeneic pregnancy (weight of spleen from virgin donors 79.9 ± 1.7 mg; in allogeneic and syngeneic pregnancy 163.3 ± 4.5 and 140.0 ± 9.8 mg, respectively; $P < 0.05$); the weight of the thymus was reduced throughout pregnancy.

Weakening of the activity of the lymphocytes in the GVHR in allogeneic pregnancy can be explained by several factors: a) increased production of glucocorticoids and sex hormones and the appearance of placental hormones with an immunosuppressive action [5, 6]; b) the effect of specific blocking antibodies against maternal lymphocytes produced by the fetus [7]; c) a redistribution of the T lymphocytes during pregnancy. Toward the end of pregnancy the action of these factors grows weaker and, accordingly, the immunocompetence of the lymphocytes is restored.

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