

EFFECT OF ANTIBRAIN SERUM ON
MANIFESTATION OF HYPERSENSITIVITY OF
DELAYED TYPE AND ITS ADOPTIVE TRANSFER

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There are data in the literature on common antigens in T-lymphocytes and brain tissue [2-5]. It was accordingly decided to study (by means of immunologic methods) the problem of whether these common antigens of T-cells and brain tissue are connected with the function of these cells, which is manifested in the experimental production of hypersensitivity of delayed type (HDT) and its adoptive transfer.

In the investigation described below the effect of antibrain sera, which possessed anti-T activity also, on manifestations of HDT was studied.

EXPERIMENTAL METHOD

Rabbit antisera against the cerebral cortex of CBA mice (experimental sera) were obtained by double immunization. At the first injection, 0.2 ml of a mixture of different parts of brain homogenate (the suspension of cells of cortex from one brain in 2 ml physiological saline) with Freund's complete adjuvant was injected into the forepaws of rabbits. At the second injection (three weeks later), the same homogenate was injected without stimulator in a volume of 0.15 ml directly into the popliteal lymph nodes. The rabbits were exsanguinated on the 10th day after the second injection, if the titers of the sera in the complement fixation test were not lower than 1:512, using antigen diluted to a protein concentration of 1 mg/ml. Rabbit immune sera against other tissues of the same mice - antikidney, antiliver, and antilung - obtained by the method described previously, and also normal rabbit serum were used as the controls. All sera were tested for cytotoxic activity against CBA mouse sinus and bone marrow cells; the antibrain sera proved to be appreciably more toxic against sinus cells.

To assess the effect of the sera on manifestation of HDT in sensitized animals, they were injected intravenously into guinea pigs sensitized with different antigens one day before skin tests in doses of 0.05 to 0.15 ml/100 g body weight. Experiments on HDT transfer also were carried out on guinea pigs. The donor guinea pigs were sensitized with: microbial antigen - tubercle bacilli (TBC, autoclaved and dried) in a dose of 1 mg per guinea pig; serum antigen - bovine γ -globulin (BGG) in a dose of 200 μ g per guinea pig, and tissue antigen - extract of rabbit kidney in a dose of 15 μ g per guinea pig. All antigens were injected into the paws of the guinea pigs as a single dose together with Freund's complete adjuvant. Hypersensitivity was transferred by means of peritoneal exudate cells (PEC), taken from sensitized guinea pigs on the 7th day after sensitization. The PEC for transfer were treated with antitissue immune sera in vitro. To a suspension of cells in medium No. 199 one or other immune serum was added in doses of 0.05 to 0.3 ml/ 10^8 cells. The mixture was kept for 30 min at 37°C, after which the cells were washed twice to remove serum with medium No. 199 and suspended in the same medium to a concentration of 15×10^7 ml. PEC treated (or untreated) with sera were injected intravenously into the recipient guinea pigs in a dose of 5×10^8 , and 1 h after injection of the cells skin tests were performed, using the same antigen as was used to sensitize the guinea pigs donating the PEC. Solutions of tuberculosis antigen, BGG, and kidney extract in doses of 10 and 100 μ g in 0.1 ml were used for the skin tests. The tests were read after 3, 24, and 48 h.

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TABLE 1. Blocking Transfer of HDT by Antibrain and Other Antitissue Sera

Expt.	Sensitization of guinea pigs donating PEC	Sera for treatment of cells to be transferred	Dose, ml/10 ⁸ PEC	Skin reactions in guinea pigs receiving treated cells		
				strong	reduced	absent
1-4	Extract of rabbit kidney	Antibrain				
5	The same	№ 658	0,05-0,2	0	0	11/11
6	BGG	№ 658	0,025	0	3/3	0
7	TBC	№ 659	0,05	0	0	4/4
8,9	"	№ 661	0,3	0	0	3/3
10-12	BGG	№ 039	0,15-0,25	0	0	6/6
13	TBC	№ 039	0,05-0,12	0	0	10/10
14	BGG	Antikidney	0,25	2/2	0	0
		Antiliver	0,25	2/2	0	0
		Antilung	0,25	2/2	0	0
		Antikidney	0,5	3/3	0	0
		Antiliver	0,5	3/3	0	0
1, 4, 7, 11, 12	Corresponding to experiment	Antilung	0,5	1/3	2/3	0
		Normal serum	0,25-1,0	0/0	0	0

Legend. Denominator - number of animals used in experiment; numerator - number of guinea pigs with skin reactions of one or other level of intensity.

EXPERIMENTAL RESULTS

Four series of antibrain sera were studied in twelve experiments on adoptive transfer of HDT to the above-mentioned three antigens. As Table 1 shows, treatment of the cells for transfer with antibrain sera abolished the ability of the cells to transfer the state of HDT in 11 of 12 experiments, and in experiment No. 5 it reduced their activity. Preliminary treatment of the cells with control sera (antitissue and normal) did not affect adoptive transfer of HDT in 6 of 7 experiments, and only in one experiment (No. 14) did it reduce the activity of the transferred cells. It will be noted that, by contrast with the action of so-called "anti-receptor" sera, treatment of the sensitized PEC with antibrain serum was not selective with respect to the antigen with which the donor guinea pigs were sensitized, i.e., it was not specific in character.

It will be recalled that sera obtained from rabbits immunized with PEG of mice or rats taken 6-8 days after sensitization of the animals with various antigens were called "antireceptor" sera. Such sera blocked the adoptive transfer of HDT from sensitized guinea pigs to intact guinea pigs. Under these circumstances the blocking was selective with respect to the sensitizing antigen [1].

In analogous experiments serum against rat brain was tested. The results were identical with those obtained in experiments with sera against mouse brain.

Experiments were carried out to study the effect of various antitissue sera on manifestation of the allergic reaction of delayed and immediate types. Allergic reactions of immediate type were induced by intraperitoneal injection of large doses of antigen into guinea pigs, and sensitivity was tested not before three weeks later. Allergic reactions of delayed type were induced by a single intradermal immunization with small doses of antigen (10 µg protein) and sensitivity was tested in the early period after sensitization. The character of allergic reactivity was tested in several animals of the appropriate group by reproducing a general anaphylactic reaction, which was detected only in animals with allergy of immediate type.

Intravenous injection of antibrain serum (24 h before the skin test) was found to block cutaneous reactivity under HDT conditions in 4 of 7 experiments in half of the animals (14 of 28). Injection of other antitissue sera was unsuccessful. Meanwhile, under conditions of allergic reactivity of immediate type, preliminary injection of antibrain serum into the sensitized guinea pigs did not affect the result of the skin test. Injection of the antireceptor sera, however, did not give clear results.

The results of these experiments showed (Table 2) that antibrain sera against xenogeneic brain suppressed completely the adoptive transfer of HDT by lymphocytes of sensitized donors, unlike other antitissue sera. In this respect they behaved similarly to antireceptor sera, from which, however, they differed in the nonspecificity of their action. This fact suggests a difference in cell receptors in the two cases. Possibly the action of antibrain sera is connected with their general cytotoxicity toward T-cells, whereas the action of antireceptor sera is connected with the blocking of specific receptors ("effector structures"). This agrees in a large measure with the results of experiments on the prevention of local allergic reactions in sensitized guinea pigs by preliminary injection of immune sera into their blood stream. Prevention was clearly noted only in experiments with antibrain sera and was not clear when antireceptor sera were used, depending on the

TABLE 2. Effect of Rabbit Immune Sera
against Various Mouse Tissues on Manifesta-
tion of Allergic Reaction in Guinea Pigs
In experiments on adoptive transfer of HDT

Immune sera	Blocking ac- tion on cells	Specificity of blocking	Result of transfer of HDT
Antireceptor	+	+	Blocking
Antibrain	+	—	"
Antitissue	—	—	Transfer

In experiments on detection of delayed and immediate
allergic reactions in sensitized guinea pigs

Immune sera	Prevention of local allergic reactions after preliminary injection of sera	
	delayed reac- tions	immediate re- actions
Antireceptor	Action not clear	—
Antibrain	+	—
Antitissue	—	—

different character and also, evidently, the different point of application of the two sera. As might be expected, neither of these types of serum, nor the various antitissue sera, had any effect on manifestation of hypersensitivity of immediate type.

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