IMMUNE REACTION OF THE ORGANISMS TO INJECTION OF CARCINOGENS AND ANTIBODIES

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The authors showed previously that autoantigens are formed in the body under the influence of carcinogenic [4] and noncarcinogenic [3, 5] compounds. Since some investigators [1] attach great importance to autoimmune processes in the pathogenesis of cancer, further investigations have been carried out along these lines.

In the present investigation the immunologic processes arising in animals after injection of carcinogens — 2-acetylaminofluorene (2AAF), 3,4-benzpyrene, 9,10-dimethylbenzanthracene — and noncarcinogens — penicillin, streptomycin — were studied.

EXPERIMENTAL METHOD

Experiments were carried out on Wistar albino rats and rabbits.

The rats (50-75 g) received 4 mg 2AAF by mouth daily for 90 days and the rabbits received 9,10-dimethylbenzanthracene (group 1) or 3,4-benzpyrene (group 2) by intramuscular injection (both compounds in a dose of 3 mg daily for 3 days), penicillin (group 3), or streptomycin (group 4; in each case 50,000 units/kg daily for 10 days, intramuscularly).

The rats were sacrificed in batches of 10 animals at a time, 1, 5, 10, 20, and 30 days after treatment, and, thereafter, every 30 days until the appearance of tumors in the liver. The changes in the immunologic specificity of the liver proteins were studied by the reaction of anaphylaxis with desensitization in guinea pigs. Saline extracts of the liver of healthy (separately and mixed with 2AAF) rats and rats poisoned with 2AAF and from a hepatoma were used as antigens. The experiments were carried out by the author's usual scheme [3, 5].

Antibodies against the chemical preparations, the liver, and the hepatoma were determined in the serum of the rats and rabbits (in the latter on the 9th day after the end of injection of the substances) by the methods described previously [2, 3]. Antibodies against the hepatoma were determined in the serum of the rats after additional exhaustion of the serum with insoluble antigen prepared from the formalinized liver of rats receiving 2AAF for 60-90 days (the serum was mixed 1 : 1 with homogenate of the formalinized liver, stirred, and allowed to stand for 2 h at room temperature). Absorption was regarded as complete if a negative reaction was obtained with soluble antigen from the liver.

EXPERIMENTAL RESULTS

The results of the experiments on rats with 2AAF are given in Table 1.

Table 1 shows that under the influence of 2AAF, three types of antigens are formed in succession: after the 1st day the liver proteins formed a complex with the 2AAF, after the 5th day a new antigen appeared, the specificity of which was not connected with the presence of 2AAF in its molecule (this antigen was found until the end of the experiment), and on the 270th day an antigen characteristic of hepatoma appeared. Corresponding antibodies were formed against these antigens. Antibodies against the heptaoma could be found on the 120th day of the experiment.

In the overwhelming majority of rabbits antibodies were detected against the tested compounds and against the liver.

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TABLE 1. Changes in Immunologic Specificity of Liver Proteins of Rats during Feeding on 2AAF

Expt. No.	Days after 1st injection of 2AAF	Reaction of anaphylaxis					Titer of antibodies in sera of rats during reaction with test antigens			
		No. of rats	sensitizing antigen (2-4 mg)	desensitizing antigen (6 and 2 mg)	reacting antigen	severity of shock	antigen of rats' liver		hepatoma antigen	2AAF
							receiving 2AAF	healthy		
1	—	9	LAG	LAG	LAG	—	0	0	0	0
2	1	3	CAG	LAG	LAG + 2AAF	3-4+	0	0	0	0
	1	3	CAG	LAG + 2AAF	HAG	1+				
3	5	3	CAG	LAG	LAG + 2AAF	2-3+				
	5	3	CAG	LAG + 2AAF	CAG	2-3+	64	8	0	4
4	10	3	CAG	LAG	LAG + 2AAF	1-3+				
	10	3	CAG	LAG + 2AAF	CAG	2-3+	256	32	0	8
5	30	3	CAG	LAG	LAG + 2AAF	2+				
	30	3	CAG	LAG + 2AAF	CAG	2-3+	512	64	0	32
6	90	3	CAG	LAG	LAG + 2AAF	1-2+	64	16	0	16
	90	3	CAG	LAG + 2AAF	CAG	3+				
7	120	3	CAG	LAG	LAG + 2AAF	—	128	32	8	0
	120	3	CAG	LAG + 2AAF	CAG	3+				
8	270	4	HAG	CAG	HAG	1-2+	64	32	16	0
	270	4	HAG	LAG + 2AAF	HAG	2+				

Legend: LAG — antigen from liver of healthy rats; CAG — antigen from liver of rats receiving 2AAF; HAG — heptoma antigen.

Note: A water-chloroform extract of the liver of healthy rabbits and streptomycin were used as the control antigens in the reaction to detect the antibodies.

The immunological processes taking place in the animal body after administration of carcinogenic substances are thus similar (except for the last stage of carcinogenesis) to those taking place in response to the injection of antibiotics. Perhaps the carcinogen is bound to the body proteins more firmly and disturbs their structure to a greater degree. However, some authors [6] did not detect any essential differences between the binding of carcinogenic and noncarcinogenic compounds.

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