STUDY OF COMPLEMENT-FIXING ACTIVITY OF RAT SERA DURING COMPENSATORY HYPERTROPHY OF THE KIDNEY AND REGENERATION OF THE LIVER

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Compensatory hypertrophy of the kidney in rats is accompanied by the appearance of freely circulating kidney autoantibodies 24 h -8 days after the operation. During regeneration of the liver and of the kidney after partial resection of the organ no freely circulating antibodies were detected.

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An important role has been ascribed to humoral factors of immunity in the realization of repair processes [1, 7]. However, the presence of specific, freely circulating antiorgan antibodies in the serum of animals after operations has not been demonstrated. The few investigations so far carried out [2-5] do not solve this problem for various reasons.

The object of the present investigation was to study the immunologic activity of the serum and, in particular, its complement-fixing hour, in animals during regeneration of the liver and kidney.

EXPERIMENTAL METHOD

Experiments were carried out on 37 noninbred male rats weighing 250-350 g. One kidney was removed completely (series I) from 16 animals, two-thirds of the liver was removed from 11 other animals by the usual method (series II), and approximately one-third of the kidney was resected from 4 rats (series III). Three intact rats and 3 rats undergoing a mock nephrectomy served as the control. Blood was taken from the experimental animals for immunologic tests before the operation and 24, 48, and 72 h and 7-8 days thereafter. Altogether 127 sera were studied. The test used was the complement fixation test (CFT) to 100% hemolysis. Before testing, the sera were heated for 30 min at 56°. The antigens consisted of 24-h saline extracts from the organs (liver, kidney). The minced tissue was mixed with physiological saline in the proportion of 1 g/10 ml. Complement consisted of lyophilized guinea pig serum diluted 1 :10 with physiological saline. The results were expressed in + signs, using a 4-point system, after incubation of the samples at 37° and the tests were reproduced twice.

EXPERIMENTAL RESULTS

The results of the tests showed that unilateral nephrectomy is accompanied by a regular increase in the complement-fixing activity of the serum relative to extracts of the same animal's kidney. Delay of hemolysis was observed in 9 of the 16 nephrectomized rats. These changes were found between 24 h and 8 days after the operation, and they were more marked 48 h after nephrectomy. The sera of all animals used reacted to ++ and +++ in dilutions of 1 : 20, 1 : 40, and even 1 : 80. Meanwhile, the sera of none of the rats before operation, in a dilution of 1 : 20, reacted with kidney and liver antigen. Animals undergoing the mock operation or left intact, when tested after the same time intervals as those undergoing nephrec-

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TABLE 1. Complement Fixation Test on Sera of Unilaterally Nephrectomized Rats with Kidney and Liver Extract

Dilution of serum	Time after operation											
	before operation			24 h			48 h			7-8 days		
	kidney	liver	SC	kidney	liver	SC	kidney	liver	SC	kidney	liver	SC
1 : 10	+	H	H	++ (+)	H	H	++++	H	H	+++	H	H
1 : 20	H	H	H	+	H	H	-	H	H	++	H	H
1 : 40	H	H	H	±	H	H	+	H	H	+	H	H
1 : 80	H	H	H	H	H	H	±	H	H	±	H	H
AC	H	H	—	H	H	—	H	H	—	H	H	—
1 : 10	++	+	H	+++	+	H	+++	+	H	+++	+	H
1 : 20	H	H	H	++	H	H	+++	H	H	++	H	H
1 : 40	H	H	H	+	H	H	++	H	H	+++	H	H
1 : 80	H	H	H	H	H	H	+	H	H	+	H	H
AC	H	H	—	H	H	—	H	H	—	H	H	—
1 : 10	+	±	H	+++	+	H	+++	+	H	+++	+	H
1 : 20	H	H	H	++	H	H	+++	H	H	++	H	H
1 : 40	H	H	H	++	H	H	++	H	H	+	H	H
1 : 80	H	H	H	+	H	H	+	H	H	+	H	H
AC	H	H	—	H	H	—	H	H	—	H	H	—
1 : 10	++	++	H	++	++	H	++++	++	H	++	+	H
1 : 20	+	H	H	+	H	H	+++	H	H	+	H	H
1 : 40	H	H	H	+	H	H	++	H	H	+	H	H
1 : 80	H	H	H	H	H	H	++	H	H	H	H	H
AC	H	H	—	H	H	—	H	H	—	H	H	—
HSC	++++											

Legend here and in Table 2: H) complete hemolysis; + to ++++) degree of delay of hemolysis; AC) antigen control; SC) serum control; HSC) hemolytic system control.

tomy, did not exhibit delay of hemolysis during contact between the serum and antigen from kidney and liver tissues. Each experiment was accompanied by a control investigation for anticomplementarity of the antigens used. The results of the tests (Tables 1 and 2) indicate that the observed changes took place, not because of the appearance of anticomplementary properties of the serum in the nephrectomized animals, but as a result of interaction between the serum and antigen of the corresponding organ. It can be considered that compensatory hypertrophy of the kidney was accompanied by the appearance of kidney autoantibodies in the serum. The sera of nephrectomized animals did not react at these times with antigen from the liver.

Contrary to expectation, the operation on the liver was not accompanied by the appearance of liver antibodies in the serum. The serum of none of the 11 hepatectomized animals possessed complement-fixing activity relative to antigen from the kidney tissue and the same animals's liver tissue to the same extent as after unilateral nephrectomy. The nonappearance of freely circulating liver antibodies does not, in itself, prove their absence in partially hepatectomized rats. The possibility is not ruled out that the wound surface can adsorb antibodies on to a regnerating organ. After removal of a small piece of kidney, freely circulating antibodies likewise were not discovered in any of the four rats investigated. The possible reason for this phenomenon may perhaps become clearer if methods enabling antibodies fixed on organs to be detected are used.

The process of compensatory hypertrophy of the kidney is thus accompanied by the appearance of kidney complement-fixing antibodies in the blood of the experimental animals. It is especially interesting that these antibodies arise as a result of the tissue deficit, confirming the view that immune reactions can develop despite a lack of organ antigen in the body [6, 7].

TABLE 2. CFT on Serum of Intact Rats and Rats Undergoing Mock Operation with Kidney and Liver Extract

Dilution of serum	Control No. 1 (mock operation)									Control No. 2 (cardiac puncture)								
	before operation			time after operation						before puncture			time after puncture					
				24 h			48 h						24 h			48 h		
	kidney	liver	SC	kidney	liver	SC	kidney	liver	SC	kidney	liver	SC	kidney	liver	SC	kidney	liver	SC
1 : 10	+	±	H	+	+	H	+	+	H	H	H	H	±	±	H	±	±	H
1 : 20	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
1 : 40	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
1 : 80	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
AC	H	H	—	H	H	—	H	H	—	H	H	—	H	H	—	H	H	—
1 : 10	++	±	H	+	±	H	±	±	H	H	H	H	H	H	H	+	H	H
1 : 20	±	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
1 : 40	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
1 : 80	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
AC	H	H	—	H	H	—	H	H	—	H	H	—	H	H	—	H	H	—
1 : 10	+	H	H	+	H	H	+	H	H	H	H	H	H	H	H	H	H	H
1 : 20	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
1 : 40	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
1 : 80	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
AC	H	H	—	H	H	—	H	H	—	H	H	—	H	H	—	H	H	—

HSC ++++

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