

# $\alpha$ -FETOPROTEIN IN RAT SERA AFTER PARTIAL HEPATECTOMY

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The sera of rats after partial hepatectomy were investigated by immunoautoradiography. An  $\alpha$ -fetoprotein was discovered 48 h after the operation, and its concentration decreased until the 12th day after the operation.

$\alpha$ -Fetoprotein ( $\alpha$ -fp) is a specific component of embryonic serum synthesized by the embryonic liver [2, 6].

In the adult organism, synthesis of  $\alpha$ -fp is resumed in tumors of hepatocellular origin [1, 4, 5].

Conflicting data have been obtained concerning the resumption of  $\alpha$ -fp synthesis in the regenerating liver. One investigation, for instance, showed that regeneration of the liver in adult mice is accompanied by the appearance of  $\alpha$ -fp in the blood. However, attempts to reproduce these findings in adult rats were unsuccessful [4, 8]. The ability of synthesize  $\alpha$ -fp after hepatectomy in rats has been observed only in very young animals, in the 5th week of life, during the first week after its disappearance from the serum [4].

However, the absence of  $\alpha$ -fp from the sera of adult rats after partial hepatectomy must not be regarded as firmly established, for the sensitivity of the agar diffusion test used was probably too low to enable its detection.

It is particularly important to discover whether  $\alpha$ -fp is synthesized during regeneration of the liver because of the fact that the appearance of  $\alpha$ -fp is used in clinical practice as a specific diagnostic test for primary carcinoma of the liver and for teratocarcinoma.

In the present investigation the method of immunoautoradiography, which has much higher sensitivity, was used to detect  $\alpha$ -fp in the sera of rats after partial hepatectomy.

## EXPERIMENTAL METHOD

Laboratory rats weighing 115-218 g were used. Partial hepatectomy was performed by the method suggested by Higgins and Anderson [7]. Blood was taken from the retroorbital sinus of the eye before and 12 days after the operation on the rats. Laparotomy was performed on another group of five rats, and blood was taken from these animals at the same times as hepatectomized rats.

$\alpha$ -Fetoprotein was determined by immunoautoradiography. A test system kindly provided by A. I. Gusev and A. K. Yazova was used for the precipitation test. The serum of a rabbit immunized by a partially purified sample of rat  $\alpha$ -fp by a method described previously [3] was used as the antiserum in this test system, and the antigen was the serum of newborn rats.

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TABLE 1.  $\alpha$ -Fetoprotein in Sera of Rats after Partial Hepatectomy

No. of animals	Sex	Weight in (g)	Results of determination of $\alpha$ -fetoprotein								
			before operation	after operation							
				24 h	48 h	72 h	96 h	120 days	7 days	9 days	12 days
1	♂	120	—	—	+++	+++	+++	+++	.	.	.
2	♂	215	—	—	+++	+++	+++	+++	.	.	.
3	♂	190	—	—	+++	+++	+++	+++	.	.	.
4	♂	123	—	—	++++	+++	+++	+++	.	.	.
5	♂	148	—	—	++++	+++	.	.	.	.	.
6	♂	159	—	—	++++	+++	.	.	.	.	.
7	♂	177	—	—	++++	+++	.	.	.	.	.
8	♂	218	—	—	++++	+++	.	.	.	.	.
9	♂	204	—	—	++++	+++	.	.	.	.	.
10	♂	180	—	—	++++	+++	.	.	.	.	.
11	♂	140	—	—	++++	+++	+++	+++	.	.	.
12	♂	192	—	—	++++	+++	+++	+++	.	.	.
13	♂	183	—	—	++++	+++	+++	+++	.	.	.
14	♂	182	—	—	++++	+++	+++	+++	.	.	.
15	♂	170	—	—	++++	+++	+++	+++	.	.	.
16	♂	181	—	—	+++	+++	+++	+++	.	.	.
17	♂	153	—	—	+++	+++	+++	+++	.	.	.
18	♂	181	—	—	+++	+++	+++	+++	.	.	.
19	♂	157	—	—	+++	+++	+++	+++	.	.	.
20	♂	181	—	—	+++	+++	+++	+++	.	.	.
21	♂	155	—	—	+++	+++	+++	+++	.	.	.
22	♂	202	—	—	+++	+++	+++	+++	.	.	.
23	♂	177	—	.	+++	.	.	.	+++	+++	—
24	♂	123	—	.	+++	.	.	.	+++	+	—
25	♂	147	—	.	+	.	.	.	+++	+	—
26	♂	146	—	.	+	.	.	.	+++	+	—
27	♂	154	—	.	+++	.	.	.	+++	+	—

Note: —no  $\alpha$ -fp found in serum; +  $\alpha$ -fp found in serum; •  $\alpha$ -fp not tested for.

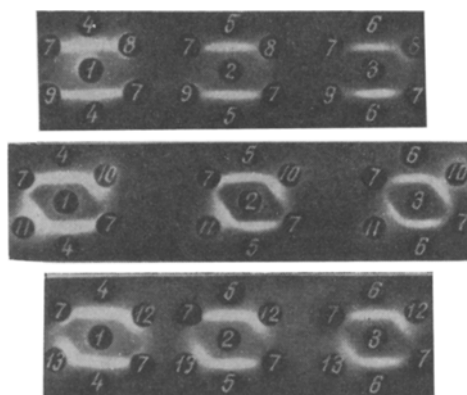


Fig. 1. Detection of  $\alpha$ -fp in serum by immunoautoradiography. 1) Antiserum of test system (AS) in dilution 1 : 8; 2) AS in dilution 1 : 16; 3) AS in dilution 1 : 32; 4) antigen of test system (AG) in dilution 1 : 8; 5) AG in dilution 1 : 16; 6) AG in dilution 1 : 32; 7) physiological saline; 8-13) test sera of rats: 8) before partial hepatectomy; 9) 24 h, 10) 48 h, 11) 72 h, 12) 7 days, and 13) 9 days after hepatectomy.

content of  $\alpha$ -fp decreased in samples of sera taken on the 7th and 9th days, and by the 12th day after the operation it was only found in traces.

As a control of specificity, the sera of five rats undergoing laparotomy were tested. No  $\alpha$ -fp was found in any sample of these sera.

By the use of the method of immunoautoradiography, which considerably increases the sensitivity of the agar diffusion reaction (by about 50 times) it could thus be shown that regeneration of the liver in adult rats is accompanied by the appearance of  $\alpha$ -fp in their serum.

The test system was taken in optimal dilutions for ordinary precipitation and then diluted 8, 16, and 32 times. The test sample of serum was studied with each of the three test systems by the method described previously [5a].

The content of  $\alpha$ -fp in the test samples was estimated from the presence of a reaction with 1, 2, or 3 of the test systems. If  $\alpha$ -fp was present in excess relative to the antiserum, the result was described as +++. The reaction was called +++ if the  $\alpha$ -fp in the test samples reacted with all three test systems, ++ if it reacted with two, and + if it reacted with one test system.

## EXPERIMENTAL RESULTS

Partial hepatectomy was performed on 27 rats. The results given in Table 1 show that before the operation no  $\alpha$ -fp was discovered in the serum of the rats (Fig. 1). It appeared 48 h after the operation. On the following day there was no decrease in the quantity of  $\alpha$ -fp detected, and it remained at approximately the same level until the 5th day after the operation. The

However, the level of  $\alpha$ -fp in the blood of rats with a regenerating liver was much lower (by about 50-100 times) than in mice. In both cases the appearance of  $\alpha$ -fp is only temporary in character. The  $\alpha$ -fp concentration reached a maximum on the 2nd-3rd day after the operation and then decreased over a period of about 2 weeks.

These results indicate that  $\alpha$ -fp is formed during regeneration of the liver in both mice and rats, and it is evidently a common phenomenon. These results must be taken into consideration when highly sensitive methods of  $\alpha$ -fp detection are used for the diagnosis of carcinoma of the liver in man.

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