ACTION OF BLOOD PLASMA OF PARTIALLY HEPATECTOMIZED RATS ON MITOSES IN THE LIVER OF INTACT RECIPIENT RATS

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According to reports in the literature, if the blood serum or plasma of partially hepatectomized animals is injected into intact or partially hepatectomized recipients, stimulation of cell division is observed in the liver of the recipients [2, 6, 11, 12]. If the liver of one of a piar of parabiotic partners is partially removed and then regenerates, the mitotic activity of the liver cells of the other partner is often increased [4]. These experiments suggested that in the process of regeneration certain hormones regulating cell division appear in the blood.

In some cases, however, the stimulant action of serum or plasma of partially hepatectomized donors on the mitotic activity in the liver of intact or partially hepatectomized recipients was not observed [7, 9, 10], or cell division was inhibited [3]. Some investigators are inclined to attribute these different effects to differences in the experimental conditions (age of the animals, time of performing the operations and giving the injections, volume of tissue removed, time elapsing after the operation, composition of the diet, etc.) [5, 8].

The object of this investigation was to study the action of the blood plasma of hepatectomized donors on mitosis in the liver of intact recipients, when the operations on the donors were performed at different times and the plasma obtained was stored for different periods of time.

EXPERIMENTAL

Two series of experiments were carried out on noninbred female albino rats weighing 150-170 g and in both series the animals were divided into donors and recipients. The donors were intact and partially hepatectomized (about 65% of the liver was removed) rats. The recipients were intact animals. In the experiments of series I partial hepatectomy was performed on the donors at 8 a.m. and the rats were exsanguinated 32 h later (at 4 p.m.). In series II the operation was performed at 4 p.m. and the animals exsanguinated 40 h later (at 8 a.m.). The intact donors were bled at the same time as the hepatectomized animals. In every case, blood was taken from the abdominal aorta and sodium citrate was added. The plasma was obtained from the blood and injected intraperitoneally into the two respective groups of recipients. Before use, the plasma was kept at 7° (for 14 h in the experiments of series I and for 24 h in series II). The injections were given next day at 7 a.m. (3 ml plasma) and at 2 p.m. (1 ml plasma) to each recipient. The recipient rats were sacrificed 48 h after the first injection (at 7 a.m.) and the liver was fixed for subsequent histological examination. The mitoses were counted in not less than 1500 cells in preparations (7 μ thick, stained with Mayer's hematoxylin and eosin) from each animal. The mitotic coefficient was calculated in promille.

EXPERIMENTAL RESULTS

The results are given in the table. They show that in the experiments of series I the mitotic coefficient (MC) in the liver of the 11 recipient rats of group B (injections of plasma from hepatectomized donors) was higher than the MC of the corresponding animals of the control group A (injections of normal plasma). In the remaining animals of both groups the MC was zero. The MC in the liver of the first two animals of group B was almost twice as high as the maximal MC in the controls.

The difference between the MC in the liver of the animals of groups A and B was statistically significant ($P = 0.01$). In these experimental conditions, therefore, injection of the plasma of the partially

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Effect of Plasma of Intact and Hepatectomized Rats on Mitotic Activity in the Liver of Intact Recipients (mitotic Coefficient in %)

Rat No.	Experiments of series I		Experiments of series II	
	group A (plasma of normal rats injected)	group B (plasma of hepatectomized rats injected)	group A (plasma of normal rats injected)	group B (plasma of hepatectomized rate injected)
1	0,66	1,08	0,69	0,54
2	0,44	1,05	0,49	0,26
3	0,06	0,63	0,37	0,23
4	0,06	0,51	0,15	0,21
5	0,06	0,49	0,08	0,20
6	0,06	0,23	0,08	0,19
7	0,05	0,22	0,08	0,15
8	0,05	0,21	0,07	0,14
9	0	0,07	0,07	0,14
10	0	0,07	0,07	0,14
11	0	0,07	0	0,08
12	0	0	0	0,08
13	0	0	0	0,05
14	0	0	0	0
15	0	0	0	0
16	—	0	—	0
Mean	0,10±0,05	0,29±0,05	0,14±0,05	0,15±0,03
P	0,01		0,85	

hepatectomized donors caused an increase in the mitotic activity in the liver of the intact recipients (compared with the injection of normal plasma).

In the experiments of series II (see table) the MC in the liver of the first three animals of group B was lower than the MC of the corresponding control animals. Although the MC in the remaining rats of group B was higher than this index in the liver of the control animals, the differences between the values of this coefficient in these two groups were not significant (P = 0.85). The plasma of the hepatectomized animals thus did not stimulate cell division.

It is difficult as yet to explain the reason for the disparity between the results of these two series of experiments. It can only be surmised that differences in the experimental conditions had some part to play in it.

In series I, for instance, partial hepatectomy was performed at 8 a.m. and bleeding took place at 4 p.m., while in series II the operation started at 4 p.m. and the animals were bled at 8 a.m. Possibly by performing hepatectomy in the morning and bleeding the animals in the afternoon, the resulting plasma contained a higher concentration of the factors stimulating cell division, than when the operation was performed in the afternoon and the donors bled in the morning. This suggestion is in agreement with results reported in the literature [1], showing that during reparative regeneration of the liver in mice the numbers of mitoses in the liver is dependent on the time of performance of the partial hepatectomy (there were more mitoses in the liver after morning than after afternoon operations).

However, the reason for the disparity between the results of these two series of experiments could have been differences in the plasma storage time (14 h in series I, 24 h in series II). On the assumption that the active humoral factors are unstable and that their activity is reduced by the action of temperature, depending on the duration of storage, the following hypothesis may be submitted: in the experiments of series II the activity of the factors was reduced so much that they had no detectable effect on the mitotic activity of the liver of the intact recipients.

Another possibility is that 40 h after the operation the concentration of factors stimulating cell division in the blood of the hepatectomized donors was less than 32 h after the operation, so that in the experiments of series I stimulation of mitotic activity was observed in the recipients' liver, whereas in series II this effect was absent.

It is evident that for the nature of the humoral factors to be studied in detail the correct experimental conditions must be worked out in which the action of these factors on cell division could be reproduced from one experiment to another.

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