CHANGES IN THE HEPATIC VESSELS OF ALBINO RATS AFTER EXPERIMENTAL INTERFERENCE WITH DRAINAGE FROM THE HEPATIC VEINS

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After experimental interference with the drainage of blood along the hepatic veins in albino rats (by measured narrowing of the caudal vena above the liver), in the early stages widening of the lumen and an increase in the tangential tension of the wall take place in the hepatic veins (the outflow system) and branches of the portal vein and hepatic artery (the inflow system). This stage is replaced by an increase in the muscular mass of the tunica media of these vessels and by narrowing of their lumen and an increase in the resistance to the blood flow.

The object of this investigation was to use an experimental model simulating disturbance of the venous drainage from the liver to test the hypothesis that hypertrophy of the vessel wall must be preceded by a stage of dilation of the lumen of the vessel [3, 4, 5] and to study changes in the structure of the inflow and outflow channels of the liver in the acute and subacute stages. Histological and morphometric methods also were used to examine some aspects of the mechanism of vascular reactions to venous stasis. The literature on the first of these problems is inadequate for vessels of the muscular type, and the data so far published on the second and third problems are contradictory [1, 2, 6, 7, 8, 9].

TABLE 1. Diameter of Lumen and Thickness of Walls of Intrahepatic Blood Vessels (in μ) after Disturbance of the Drainage of Blood via the Posterior Vena Cava (M ± m)

Time after ligation (in days)	Number of branches in 100 fields of vision		Branches of hepatic veins		Branches of portal vein		Branches of hepatic artery	
	hepatic	portal	lumen	thickness of wall	lumen	thickness of wall	lumen	thickness of wall
Control								
	50±0,7	15±5,0	35±1,1	2,5±0,2	29±1,4	2,6±0,2	6,1±0,7	4,0±0,4
Ligation of vena cava								
1	44±7,0	28±4,2	47±2,7	3,4±0,1	43±2,6	3,7±0,1	12,0±0,8	3,5±0,2
4—6	37±9,5	35±8,5	29±1,8	3,7±0,3	20±2,0	4,8±0,4	7,0±0,5	4,0±0,4
10—13	62±8,5	30±3,5	44±2,1	4,0±0,19	26±1,9	4,3±0,1	9,0±0,9	4,2±0,2
15—30	73±2,9	21±3,6	68±4,3	4,0±0,2	44±4,2	4,4±0,3	8,5±1,0	5,5±0,7
45—60	89±18,0	29±1,6	56±3,8	4,7±0,3	63±9,6	4,0±0,2	8,5±1,0	5,5±0,7
90—210	—	—	53±3,4	—	50±8,1	—	9,2±1,4	7,5±0,8
Administration of chloramphenicol								
21	99±32,0	27±4,0	43±3,9	2,0±0,1	39±3,6	2,4±0,1	9,1±1,2	3,7±0,5
Administration of aurantin								
10	73±2,0	45±4,8	35±1,6	2,7±0,2	37±4,0	2,5±0,2	7,4±0,9	3,2±0,3

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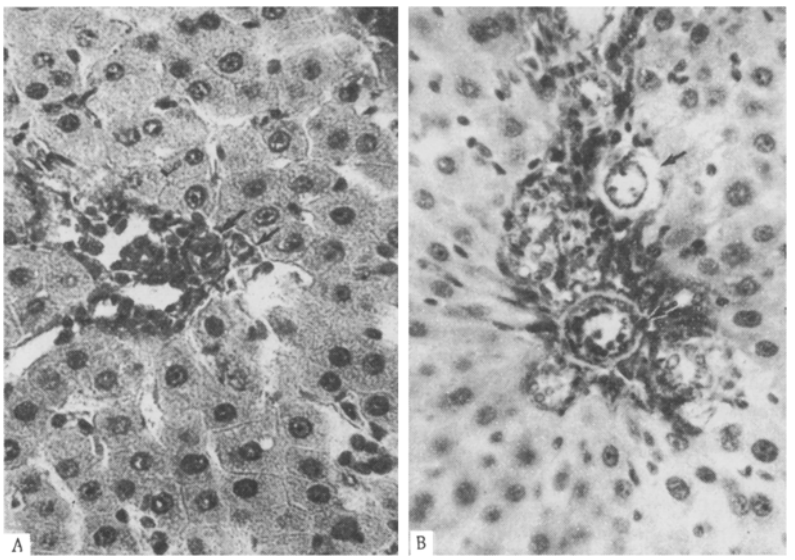

Fig. 1. Branches of the hepatic artery: A) intact rat; B) 21 days after disturbance of the venous drainage along the hepatic veins. Marked thickening of the muscular coat is observed. Fuchselin; counterstaining by Van Gieson's method, 500×.

EXPERIMENTAL METHOD

In experiments on male Wistar albino rats weighing 200-220 g measured constriction of the caudal vena cava was produced above the diaphragm, by means of a silk ligature on a catheter, down to 1.2-1.4 mm (normal diameter of the lumen 4.0-4.5 mm). Eight intact rats from the same batch were sacrificed as controls. Five rats were killed 24 h after constriction, three rats 4-5 days, five rats 10-13 days, five rats from 3 weeks to 1 month, three rats 2-3 months, and five rats 4.5-6 months after the constriction operation. Three rats undergoing the operation received aurantin, an inhibitor of RNA synthesis, in a dose of 0.33 μg/g body weight on alternate days. These animals were sacrificed on the 10th day after constriction; two animals received chloramphenicol (an inhibitor of protein synthesis) in a daily dose of 100 mg for 3 weeks.

Before sacrifice, one experimental rat from each series and one control rat received an injection of 0.5 cm^3 black ink into the femoral vein. Sections were stained with hematoxylin-eosin, with fuchselin with counterstaining by Van Gieson's method, and by Heidenhain's azan method. With a screw-operated ocular micrometer the thickness of the walls and the lumen of the intrahepatic branches of the hepatic artery and the portal and hepatic veins were measured in each section. The number of transversely divided branches of the hepatic and portal veins was counted in 100 fields of vision of 10× objective. On the basis of these results, the weighted arithmetic mean and the weighted mean error of the arithmetic mean were calculated for each time of the experiment.

EXPERIMENTAL RESULTS

The results of the measurements are given in Table 1. Until the fourth day after constriction, marked dilatation of the liver sinusoids corresponding to the inner third of the lobule was observed. At this time no ink penetrated into the sinusoids. After 10-12 days the sinusoids remained dilated, and ink was detected in some of them (with a subcapsular localization). After 3-4 weeks the picture of the sinusoids corresponded to that in the control animals.

Analysis of the numbers of transversely divided vascular branches per 100 fields of vision (Table 1) showed that from the 10th day after the operation an increase took place in the number of branches of the hepatic veins (50.0 ± 0.7 in the control, 73.0 ± 2.9 in the experimental group on the 15th-30th day after the operation). This process is associated primarily with the conversion of the dilated sinusoids into venules. The conversions in the portal venous system are less substantial.

On the first days after the operation the branches of the hepatic veins were dilated (47.0 ± 2.7 μ compared with 35.0 ± 1.1 μ in intact rats; $P < 0.001$). This dilatation was followed by a transient decrease in the

mean diameter of the lumen of the veins, and by the 10th-13th day and later a secondary dilatation of the branches of the hepatic veins developed. Parallel with these changes, after the first few days there was a statistically significant increase in thickness of the walls of the branches of the hepatic veins on account of the more powerful development of the muscular coat; after the 30th day sclerosis began to occur in the walls of these venous branches.

The branches of the portal vein also were dilated on the first day after the operation (Table 1). This dilatation was followed by constriction of the portal branches on the fourth to 15th days after disturbance of the venous drainage. By the end of the first month a secondary dilatation of the branches of the portal vein began. Besides changes in their lumen, after the 10th day there was a significant increase in thickness of the muscular coat of the branches of the portal vein.

Branches of the hepatic arteries were greatly dilated on the first day after disturbance of the venous drainage ($12.0 \pm 0.8\ \mu$ compared with $6.1 \pm 0.67\ \mu$ in the control). This was followed by some constriction of the lumen of the arteries ($4.0 \pm 0.4\ \mu$ in control animals and $7.5 \pm 0.8\ \mu$ months after the operation; Fig. 1A, B). These facts indicate an increased resistance of the arteries to the blood flow in the subacute and chronic stages of adaptation of the vessels after disturbance of the venous drainage along the hepatic veins. After injection of the inhibitors chloramphenicol and aurantin, no increase in the muscular mass in the walls of the venous branches took place, and severe dilatation of the sinusoids was accompanied by hemorrhages into the liver tissue. Against the background of aurantin injections perivenous sclerosis was observed.

After disturbance of the venous drainage along the hepatic veins in albino rats a transient dilatation of the lumen of branches of the venous collectors and of the hapatic artery thus takes place within the first few hours after the operation. These changes are accompanied by dilatation of the microcirculatory channels, indicating an increase in the lateral pressure on the wall of the blood vessels. This dilatation is superseded by constriction of the lumen and thickening of the walls on account of growth of the muscular mass in branches of the portal vein, by transient constriction and a progressive thickening of the wall on account of growth of the muscular mass and subsequent sclerosis in branches of the hepatic veins, and by an increase in the muscular mass with a tendency toward constriction of the lumen in the branches of the hepatic artery.

These results confirm previous views regarding the existence of a phase of constriction of the veins when the venous drainage is disturbed [1] and regarding the structurally distinguishable increase in resistance of the inflow channels when the outflow is disturbed. In the experiments now described these remarks apply both to the system of the portal vein, which is an inflow collector in relation to the hepatic veins, and to the system of the hepatic arteries. The results of experiments in which the inhibitors were injected confirm the compensatory character of these adaptations. These experiments also confirm the view that the response of hyperplasia and hypertrophy of the vessel wall is preceded by a stage of dilatation of the lumen and of an increase in the tangential tension of the vessel wall.

As regards the mechanism of these systemic vascular reactions, the results of these experiments can be more completely explained by the myogenic hypothesis of autoregulation of the blood supply to an organ [8, 9, 10], and in particular the existence of stages in the changes in the lumen of the vessels can be understood: the transient stage of dilatation of the lumen is superseded by constriction; this corresponds to participation of the microcirculatory system in the early stages of disturbance of the venous drainage.

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