RELATIONSHIP BETWEEN DISTURBANCE OF THE BLOOD AND LYMPH FLOW IN CARBON TETRACHLORIDE POISONING

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CCl_4 was injected into the portal venous system of dogs. The lymph flow from the thoracic duct and the pressure in the hepatic artery, portal vein, and inferior vena cava were subsequently measured. In control experiments the afferent and efferent veins of the liver were closed alternately. CCl_4 caused an increase in the portal pressure and lymph flow. The lymph flow was also increased after compression of the hepatic veins, i.e., as a result of the toxic action of CCl_4 the direct cause of the increase in the lymph flow is obstruction to the drainage of blood, with a subsequent increase in the portal pressure.

Besides an increase in the portal pressure, changes in the lymph flow in the liver are observed in CCl_4 poisoning [1-4, 7, 8]. There is also a marked discharge of ascites fluid during perfusion of the isolated liver when the pressure in the portal veins is raised as the result of occlusion of the efferent vessels [6]. On the other hand, after occlusion of the portal vein the diameter of the lymphatic collectors of the liver is reduced, they become shorter, altered in shape, and reduced in number [5]. The fact that a simultaneous increase in portal pressure and lymph flow is observed in CCl_4 poisoning suggests a casual relationship between them.

The object of the present investigation was to determine the role of elevation of the portal pressure in the increase in lymph flow in CCl_4 poisoning.

EXPERIMENTAL METHOD

Experiments were carried out on 22 dogs, including nine controls.

In acute experiments on dogs the hepatic artery, portal vein, inferior vena cava, and thoracic duct were catheterized. After repeated measurements of the initial pressure in the catheterized vessels and calculation of the initial lymph flow, CCl_4 was injected in doses of 1 ml every 10 min (10-12 ml altogether) into the portal vein. Meanwhile, the same measurements as in the control experiments were repeated at intervals of 3 min for 3-5 h (until death of the animal). Liver biopsy (from the left lateral and right medial lobes) was carried out before administration of CCl_4 and at the peak of the circulatory disturbances.

EXPERIMENTAL RESULTS

In five control experiments without administration of CCl_4 the pressure in the portal vein for 3-5 h was 84 ± 19.4 mm water, in the inferior vena cava 46 ± 16.3 mm water, and in the hepatic artery 76 ± 19.2 mm Hg, while the lymph flow was 6.6 ± 1.6 drops/min. During the 3-5 h that the experiments lasted, the parameters studied thus varied within normal limits.

Immediately after injection of 2 ml CCl_4 the pressure in the portal vein rose on the average from 81 ± 17.2 to 146 ± 41.6 mm water ($P < 0.001$), while the arterial pressure fell from 80 ± 19.5 to 50 ± 14.3

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mm Hg ($P < 0.001$). Meanwhile, the lymph flow in the thoracic duct was trebled (from 6.4 ± 1.3 to 18.5 ± 3.4 drops/min; $P < 0.001$).

Although initially transparent, the lymph became tinged with blood and pink in color after injection of 2 ml CCl_4. The liver swelled and became conjected. During administration of the CCl_4 the portal venous pressure rose further to 174 ± 5 mm water. The arterial pressure continued to fall, reaching 35 ± 9.4 mm Hg. Against the background of these changes in the hemodynamics, the lymph flow from the thoracic duct was increased 5-6 times (to 27.6 ± 1.5 drops/min). The intensity of the blood staining of the lymph increased, and by the end of the experiment the lymph was hard to distinguish from blood by its appearance. The pressure in the inferior vena cava showed no significant changes at any time during the experiment.

In biopsy specimens taken from the liver at the peak of the changes, dilatation and hyperemia of the sinusoids and diapedesis of erythrocytes into Desse's spaces were observed. Greatly dilated lymphatics were seen around the collecting veins which were either dilated or, frequently, in spasm, the interstitial tissue was edematous, and multiple diapedetic hemorrhages were present. There was a smaller increase in the diameter of the lymphatic capillaries around the dilated portal vessel. In areas of the parenchyma the structural pattern was lost and foci of necrosis were observed.

In view of these results it was decided to undertake control experiments in which the portal pressure was changed by disturbing the outflow of venous blood from and its inflow to the liver. For this purpose, after determination of the initial lymph flow, the portal or hepatic veins were alternately compressed for 15 min in four experiments and the lymph flow was recorded during this procedure.

Compressing the portal vein reduced the lymph flow on the average from 7.75 ± 1.71 to 3.75 ± 0.005 drops/min ($P < 0.01$). When the blood flow through the liver was restored, the lymph flow rose sharply to reach 23.2 ± 0.93 drops/min. On reapplication of the clamp to the portal vein the response was the same as before: the lymph flow was reduced to 10.5 ± 0.84 drops/min. On the other hand, clamping the hepatic veins in these same experiments doubled the lymph flow (from 23.2 ± 0.93 to 43.5 ± 0.95 drops/min; $P < 0.001$).

After injection of CCl_4 the portal pressure thus rose significantly. The results of morphological investigations suggest that this may be due to disturbance of the outflow of blood through changes in tone of the collecting veins.

Comparison of results of the control experiments in which the efferent veins were clamped and the results of the main series of experiments suggests that the immediate cause of the increased lymph flow was disturbance of the outflow of blood, leading to the development of portal hypertension.

In can thus be concluded that the increased lymph flow during the action of CCl_4 on the liver is due to blocking of the venous outflow, resulting in elevation of the portal pressure.

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