Experimental Hepatic Coma. (18958)

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While experimenting with ischemia of the liver in dogs, we observed 4 animals in comatose states which closely resembled hepatic coma in man. Two of these were fatal, 2 non-fatal. After many attempts to induce these comatose states at will, we found that a graded production of liver ischemia might result in the clinical manifestations of coma. If the increasing ischemia of the organ can be coped with by the gradually developing blood flow from collateral circulation, the animal may recover from coma.

Ischemia of the liver can be induced by gradually tying the vessels in the hepatic-duodenal ligament and diverting the blood flow from the portal vein into the vena cava (classical Eck fistula). The collateral circulation will then develop from the reversed flow in the gastro-duodenal, left gastric and phrenico-abdominal arteries(1).

Six 9 to 15 kg dogs were operated upon under nembutal anesthesia (35 mg/kg body weight) in a 2-stage procedure: 1st stage: Portal-caval anastomosis and ligation of the portal vein in the hepato-duodenal ligament (Eck fistula). 2nd stage: 24 to 48 hours later under nembutal anesthesia (only half the previous dose is now necessary) ligation of the common hepatic artery. Intensive treatment with penicillin and streptomycin was started immediately after the first stage and continued for about 7 days post-operatively. Four of the dogs were infused continuously with saline-glucose solution in order to avoid the complicating factor of hypoglycemia. Of the 2 dogs which did not receive glucose, one died in hypoglycemic convulsions. The other dog was in a subcomatose state for 36 hours and recovered. Of the 4 dogs infused with glucose, three had a non-fatal liver coma.

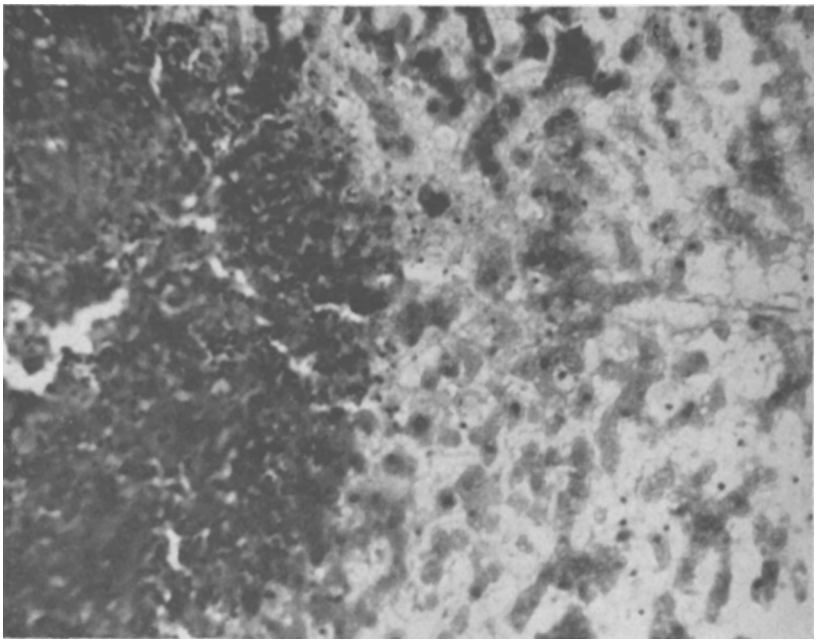

FIG. 1. Dog A64, 33 hr of fatal liver coma. (Azo-carmine aniline blue. × 300). Haemorrhagic necrosis around central vein.

1. Rappaport, A. M., *Experimental ischemia of the liver and hepatic coma. Liver Injury.* Trans. 10th Conference, May 1951. Josiah Macy, Jr. Foundation. In press.

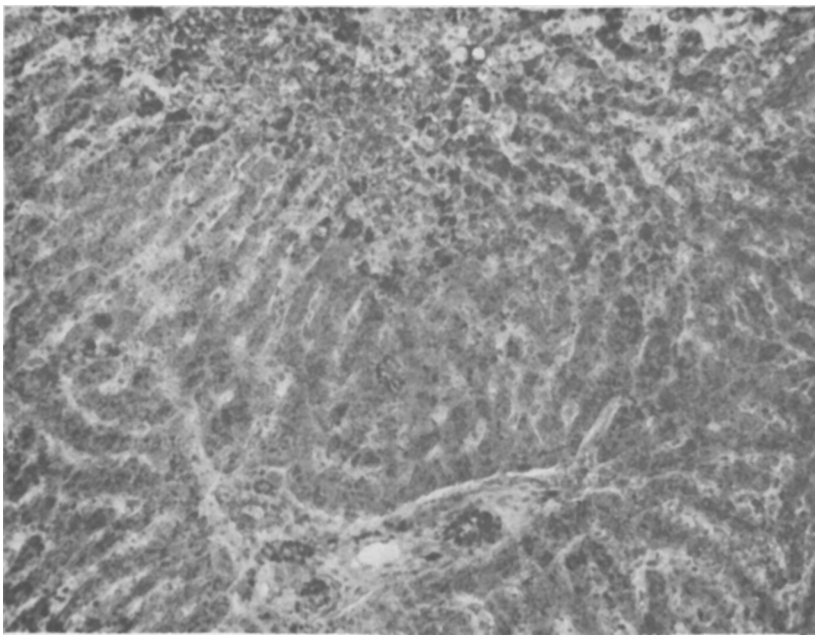

FIG. 2. Dog A69, 3 days of non-fatal liver coma. (Frozen section Oro & H × 200). Centro-lobular necrosis with slight fatty change. The parenchyma around portal area is preserved and shows little fatty degeneration.

One dog died 33 hours after the second stage operation in a deeply comatose state.

The signs displayed by the dogs were: Restlessness, loss of appetite, vomiting, sometimes tarry stools, fever, jaundice, bradycardia, stupor, ataxia, somnolence, coma with deep sonorous breathing, muscular rigidity, convulsions, and muscular twitchings (soubresauts of the French literature). Pronounced fetor hepaticus was observed in some of the dogs with advanced ischemia of the liver. However, this classical sign was not prominent in the acutely comatose animals; but this situation requires much further study.

Chemical studies have been made in the Department of Pathological Chemistry, on the blood of animals in coma and after recovery. This work will be extended and the findings will be reported.

Two of the surviving dogs showed signs of a spinal cord lesion (spastic paraplegia) 2½ to 4 weeks after they came out of coma.

The histopathological report on the liver of the dog that died in coma made by Dr. Stanley Hartroft states: "Wide central hemorrhagic necrosis occupying the entire lobule. Here and there small haloes of non-necrotic periportal parenchymal tissue are present (Fig. 1)". One dog sacrificed 3 days after it recovered from liver coma showed evidence of centro-lobular necrosis throughout. In these regions fatty change was also apparent (Fig. 2).

From our preliminary findings, we may conclude: (1) Fatal or non-fatal hepatic coma can be produced in dogs by a gradually developed ischemia of the liver. (2) This ischemia can be induced by a two-stage operative procedure: (a) Eck fistula. (b) 24 to 48 hours later, ligation of the common hepatic artery. The shorter the time interval between the two operations, the more marked the signs of liver coma. (3) Intensive postoperative treatment of the dogs with antibiotics is necessary and glucose infusion is essential. (4) Some of the dogs surviving coma show signs of a spinal cord lesion.

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