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The effect of ligation of the hepatic artery on carbohydrate metabolism.*

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In the course of some experiments on the physiology of the liver of the dog, we observed that ligation of the hepatic artery caused death of the animals in convulsions. Previous investigators[1, 2, 3] observed death in convulsions in animals after complete circulatory exclusion of the liver. Mann and Magath[4] found that after complete hepatectomy their dogs died in hypoglycemic convulsions. We, therefore, undertook the study of the relation of the blood sugar level to the convulsive seizure following ligation of the hepatic artery.

There was a remarkable constancy in the results obtained. After coming out of the anesthetic, the dogs appeared normal—walked, ran, barked, drank water and excreted normal amounts of urine and feces. The dogs remained in this apparently normal state from 15 to 50 hours, following which they became drowsy, listless, and unresponsive. Pinching or pricking did not call forth any response. The animals refused food and water. During this stage occasional fibrillary twitches were observed. Then (within 1 to 2 hours) they manifested symptoms of hyperirritability, hyper-reflexia and a sudden onset of generalized clonic convulsions followed by tonic spasms, retraction of the neck, respiratory paralysis, an occasional sharp yelp, and death. This general seizure usually lasted from 2 to 5 minutes.

* With the aid of a grant from the Therapeutic Research Committee of the American Medical Association.

1 Hahn, M., Massen, O., Nencki, M., and Pawlow, J., *Arch. für Exper. Path. u. Pharmakol.*, 1893, xxxii, 161.

2 Matthews, S. A., and Miller, E. M., *J. Biol. Chem.*, 1913, xv, 87.

3 Whipple, G. H., and Hooper, C. W., *J. Exper. Med.*, 1913, xvii, 593; *Ibid.*, 612.

4 Mann, F. C., and Magath, T. B., *Arch. Int. Med.*, 1922, xxx, 73; *Ibid.*, xxx, 171.

Coincident with these observations, the blood sugar curve was studied. It was found that there was a definite parallelism between the blood sugar level and the symptoms just described. When the blood sugar was within normal limits, the animals did did not manifest any symptoms, but as soon as it has dropped to 60 mg. per 100 cc. of blood or below, the dogs developed the first stage of the syndrome, that of drowsiness. The blood sugar dropped progressively and when it reached a level below 45 mg. per 100 cc. of blood, convulsions and death supervened.

Immediately after death autopsies were performed, and portions of the liver, skeletal and heart muscle were at once examined for glycogen. In no case were we able to find glycogen in these tissues either by alcohol precipitation or positive reduction after hydrolysis. Microscopic studies of the liver were made, the histo-pathology of which is being studied at present, but the results are not mature to be discussed at this presentation.

In a few of our animals the administration of glucose orally or intravenously was successful in bringing the animals out of convulsions and prolonging the period of survival for several hours.

To eliminate the possibility of the picture being produced by nerve injury, the plexus of nerves surrounding the hepatic artery was severed in one dog without ligating the hepatic artery. This procedure in no way interfered with the well being of the animal. The dog is still alive and normal since the operation on December 31, 1925.

CONCLUSIONS.

(1) Ligation of hepatic artery of dogs causes death in hypoglycemic convulsions.

(2) The period of survival after ligation depends upon the amount of glycogen previously stored, and varies between 15 to 60 hours.

(3) There is a total depletion of glycogen in the tissues at death.

(4) Administration of glucose prevents convulsions and prolongs life for several hours.

(5) Severing the plexus of nerves surrounding the hepatic artery does not produce this hypoglycemic syndrome.