9160

Blood Heparin and Lipid Amino N in Experimental Obstructive Jaundice.

LOUIS M. HELLMAN, ROBERT A. MOORE AND WILLIAM DEW. ANDRUS.

From the Departments of Pathology and Surgery, New York Hospital and Cornell University Medical College.

The hemorrhagic diathasis which accompanies obstructive jaundice has been a serious obstacle in the treatment of this condition. Petren[1] states that 2% of the cases of obstructive jaundice submitted to operation die of hemorrhage. In an analysis of the cases of obstructive jaundice in the New York Hospital over a period of 3 years, 50% of the operative deaths were due to hemorrhage. Walters[2] reported a similar experience.

Chemical analysis of the blood has failed to give any clue as to which patients would bleed following operation. Although the clotting time and bleeding time is increased in most instances there is no correlation between prolonged bleeding and clotting time and the hemorrhagic diathasis. Kirk and King,[3] Snell and Green,[4] Snell, Green and Rowntree,[5] Linton,[6] and Ravdin and Regal[7] concluded that the changes in the blood calcium are insufficient to explain the condition. Similarly, Moss,[8] Barke and Weir[9] found no significant variation in the fibrinogen. Doyen[10] states that the concentration of bile in the blood of subjects suffering from obstructive jaundice is insufficient to interfere with the clotting of blood. Bancroft[11] reported that the platelets of patients suffering from obstructive jaundice are normal in number and fragility. In an excellent review of the literature, Wangensteen[12] concludes that prediction of the hemorrhagic diathasis is not possible with the present methods.

---

1 Petren, G. V., *Bruns. Beiträge*, 1918, **110**, 237.

2 Walters, W., *Surg., Gyn. and Obst.*, 1921, **33**, 651.

3 Kirk, P., and King, C. G., *J. Lab. and Clin. Med.*, 1925, **2**, 928.

4 Snell, A. M., and Greene, C. H., *Am. J. Physiol.*, 1930, **92**, 630.

5 Snell, A. M., Greene, C. H., and Rowntree, L. G., *Arch. Int. Med.*, 1925, **36**, 273.

6 Linton, R. R., *Ann. Surg.*, 1931, **93**, 707.

7 Ravdin, I. S., and Regal, C., *Ann. Surg.*, 1930, **91**, 801.

8 Moss, W., PROC. SOC. EXP. BIOL. AND MED., 1931, **29**, 328.

9 Barke, C. F., and Weir, J. F., *J. Lab. and Clin. Med.*, 1933, **18**, 657.

10 Doyen, M., *Compt. rend. de la Soc. de Biol.*, 1909, **66**, 442.

11 Bancroft, F., Kugelmass, I., and Stanley-Brown, M., *Ann. Surg.*, 1929, **90**, 161.

12 Wangensteen, O. H., *Ann. Surg.*, 1928, **88**, 845.

It is significant that two basic factors concerned with the clotting of blood have never been investigated. It is the purpose of this investigation to examine the heparin and the lipid amino N in the blood of experimental animals suffering from obstructive jaundice. The greater part of the lipid amino N is cephalin.

Heparin was extracted and assayed according to the method of Howell.[13] The potency of an extract of 100 cc. of blood as compared to similar amounts of physiological saline solution was tested by mixing these with normal blood and measuring the difference in clotting times. Twelve dogs were used in pairs. In most cases several control determinations were done on both members of a pair and then one member was subjected to ligation and division of the common duct under nembutal anesthesia. Beginning one week after operation, determinations were run weekly until the death of the jaundiced animal. Van den Bergh estimations and clotting times were also done. A statistical summary of the results is shown in Table I. The difference between the amount of heparin in the jaundiced animals and the controls is less than the standard deviation of each and therefore it may be concluded that there is no significant variation in the heparin in dogs suffering from obstructive jaundice.

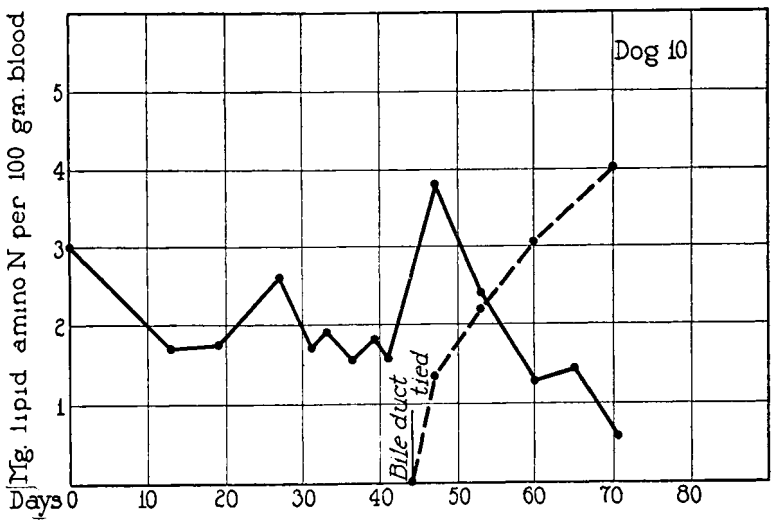
TABLE I.
Blood heparin in the dog.

Type	No. animals	No. determinations	Mean*	Standard deviation
Control	10	33	6.95	9.17
Experimental	6	23	6.72	8.22

* This figure is the delay in minutes in the clotting of blood as described in the text.

Howell[14] states that the thromboplastic substance is cephalin. In these experiments lipid amino N of whole blood has been measured by the method of Kirk, Page and Van Slyke.[15] In 4 dogs, control determinations were run. These were then subjected to ligation and division of the common duct as before. Frequent determinations were made thereafter. All determinations were run on duplicate samples, no effort being made to have the samples of more than approximately similar weight. The results on one dog, as shown in Fig. 1, demonstrate a primary rise in the lipid amino N. This is followed by a progressive fall to a level far below the normal. This

[13] Howell, W. H., *Am. J. Physiol.*, 1912, **31**, 1.
[14] Howell, W. H., *Am. J. Physiol.*, 1926, **77**, 680.
[15] Kirk, E., Page, I. H., and Van Slyke, D. D., *J. Biol. Chem.*, 1934, **106**, 203.



Lipid amino N in experimental ligation of bile duct

FIG. 1.

dog died 21 days after operation. In the second dog an attempt was made to do a cholecystoduodenostomy 33 days after the primary operation, at a time when the lipid amino N was low, and death occurred due to severe hemorrhage during the operation. In a third dog, there was a terminal rise in the lipid amino N and at autopsy there was a choledochoduodenal fistula and multiple abscesses of the liver. The fourth dog was similar to the first and second except that no initial rise after ligation of the bile ducts was seen.

In conclusion it has been shown that the circulating heparin is unchanged in obstructive jaundice in dogs. On the other hand, in uncomplicated cases there is a progressive fall of the lipid amino N of the blood, most of which is cephalin, the thromboplastic substance.