successful.

In vivo results in rabbits and cats revealed that sodium salt preparations of mactin-A and mactin-B with *in vitro* activities of approximately 100 units/mg were more active than preparations of standard 100-unit sodium heparinate. The observed intensity of action was more than 6 times that of heparin; the duration of action was also significantly greater. A satisfactory explanation for this wide discrepancy between the *in vitro* and *in vivo* activities has not been found.

As in the case of heparin the anticoagulant effect of mactin-A is neutralized by injection of protamine.

While the LD_{50} of mactin-A of 1.6 g/kg is lower than the value of 2.8 g/kg established for heparin. the anticoagulant activity of mactin-A is greater than that of heparin; therefore, the therapeutic index of mactin-A would appear to be comparable to that of heparin. Acute and chronic toxicity studies conducted thus far have revealed no apparent toxicity. Clinical trials of mactin-A and mactin-B are in progress.

Summary. Heparin-like polysaccharides with high anticoagulant activity have been isolated from 2 species of clams, *Mactra spissula* and *Artica islandica*. These purified polysaccharides, termed mactin-A and mactin-B, are related to but not identical with mammalian heparin. They possess a greater *in vivo* activity and a favorable therapeutic index when compared with heparin preparations of equal *in vitro* activity.

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Liver Regeneration: Preliminary Report.* (20093)

CHARLES G. CHILD, III, DAVID BARR, GEORGE R. HOLSWADE, AND CHARLES S. HARRISON.

From the Department of Surgical Research, Department of Surgery, New York Hospital and Cornell University Medical College, New York City.

The reason for the failure of hepatic regeneration following partial hepatectomy in dogs with Eck fistulae is not clear. Some relate this to diversion of a factor peculiar to portal blood and others simply to reduction in total blood flow through the liver. In an attempt to discover whether portal blood is essential to hepatic regeneration an operation was devised in dogs that accomplished complete diversion of the portal stream and at the same time provided the liver with a profuse supply of systemic venous blood. In this preparation the response of the liver to partial hepatectomy was studied.

Method. In one group of dogs the portal vein and inferior vena cava were divided below the liver and continuity re-established by end to end anastomosis crossing portal to systemic and caval to portal circulations. (Fig. 1). One month later 70% hepatectomy was performed. Hepatic venograms, obtained by injecting contrast material directly into the inferior vena cava, were made prior to hepatectomy to prove patency of the caval-hepatic anastomosis and to visualize the intrahepatic portal bed. Venography was repeated at intervals afterward to demonstrate regeneration *in vivo*. After periods of observation ranging from 35 to 60 days post-hepatectomy the dogs were sacrificed by exsanguination under nembutal anesthesia. Their livers were removed and weighed and the degree of regeneration calculated. The assumption was made, based upon dissections of normal livers, that a 70% hepatectomy

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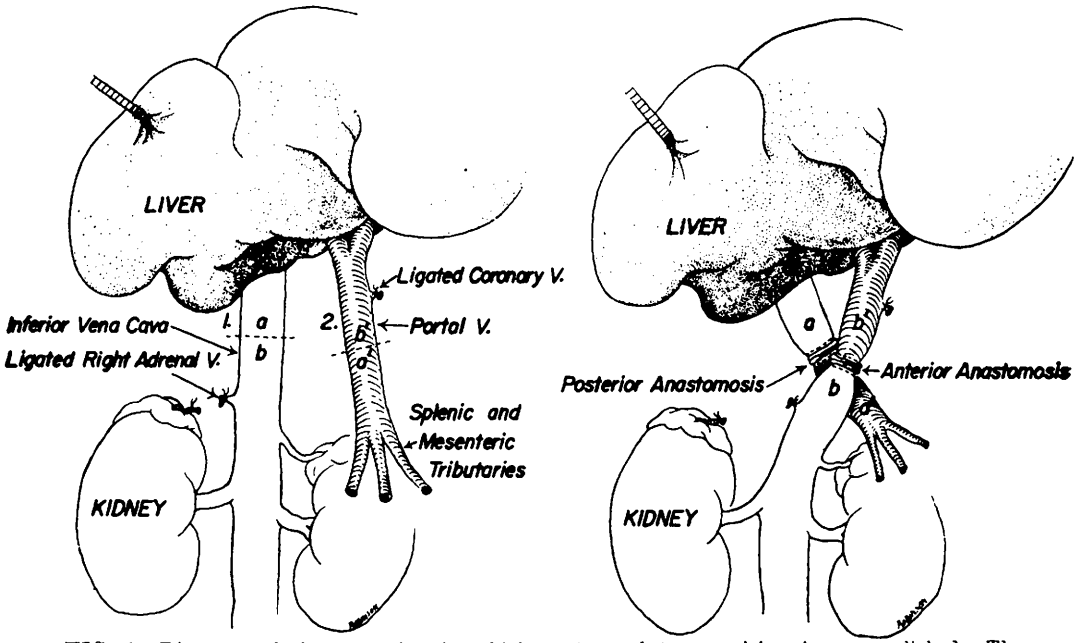

FIG. 1. Diagram of the operation in which portacaval transposition is accomplished. The inferior vena cava is divided at 1 and the portal vein at 2. The first anastomosis is performed between a and a' and the second between b and b'.

had been performed. The weight, therefore, of the operative specimen was multiplied by 3/7 to obtain the weight of the hepatic remnant, which, when subtracted from the weight of the liver removed at autopsy gave an estimate of the increase in liver weight during the experimental period. The gain was divided by the weight of the liver removed at operation and multiplied by 100 to express regeneration in per cent. Thus if gain in liver weight equalled the weight of liver removed at operation, regeneration would be 100%. Partial hepatectomy was also carried out in dogs with normal hepatic circulation and with end to side portacaval shunts. X-rays were not taken but similar calculations were made.

Results. Eight dogs survived portacaval transposition and partial hepatectomy without incident. In all regeneration observed in the venograms was striking. When the venograms made prior to partial hepatectomy were compared with those taken at intervals afterward it was clear that there was a great increase in the area and density of liver filled with contrast material. The main branches of the portal vein were enlarged. Regeneration ranged from 20 to 80% with an average of 50% (S. D. 21). (Table I).

Three normal dogs survived partial hepatectomy. Regeneration ranged from 53 to 114% with an average of 75% (S. D. 34).

Only one dog with an Eck fistula survived partial hepatectomy long enough to be considered comparable. Regeneration was not found.

Discussion. The assumption that liver regeneration has occurred is based upon two lines of evidence, the venograms and the calculations of per cent regeneration. The venograms show that the liver casts a larger and more dense shadow after partial hepatectomy than before. This is interpreted as indicative of hepatic regeneration. The calculations of per cent regeneration are less easily evaluated because of pitfalls inherent in the method. The estimate of gain in liver weight during the post-hepatectomy period is based upon the measured weights of liver removed at operation and at autopsy and the assumption that a 70% hepatectomy had been performed. In support of this assumption it was found in dissections of normal livers that the portion of liver resected constituted 71% of the total weight of the liver

TABLE I. Hepatic Regeneration Following Partial Hepatectomy in 8 Dogs with (A) Portacaval Transposition, (B) 3 Dogs Normal Hepatic Circulation, and (C) 1 Dog Eck Fistula.

Wt of dog at part. hepatect., kg	Wt of liver removed, g	Estim. wt of hep. remnant, g	Wt of dog at autopsy, kg	Wt of liver at autopsy, g	Estim. gain in liver wt, g	Interval between op. and autopsy, days	Liver regeneration, %
A. Portacaval transposition							
15.5	273	117	13.6	302	185	38	68
16.1	302	130	15.2	371	241	36	80
13.6	335	143	12.3	230	87	60	25
10.8	251	108	9.3	159	51	50	20
11.1	201	81	9.6	177	96	50	49
10.2	159	68	9.3	161	93	45	59
21.5	322	138	18.2	320	182	45	57
15.4	272	117	14.3	230	113	35	42
						Avg regeneration 50% ± S.D. 21	
B. Normal hepatic circulation							
11.4	279	120	10.4	285	165	42	59
12.3	348	147	12.9	322	185	57	53
13.9	208	89	15.0	337	238	30	114
						Avg regeneration 75% ± S.D. 34	
C. Eck fistula							
16.1	421	181	10.7	174	—7	29	0

(±S. D. 4). The liver removed at operation, however, contained an unknown quantity of blood whereas the liver removed at autopsy contained very little. The estimate, then, of the weight of liver left at operation must be unduly high and the weight of the postmortem specimen low by comparison. These considerations fix the error of gain and per cent regeneration on the low side but since each group of animals were similarly treated the error must be fairly constant.

The figures show that considerable regeneration did occur in the dogs with portacaval transposition though to a somewhat lesser degree than in the normal dogs. Whether this difference in response to partial hepatectomy is apparent or real must await the accumulation of more data. At this time the reasons for this discrepancy remain speculative.

The hepatic regeneration observed in the dogs with portacaval transposition is regarded as significant for it is well established that normal dogs(1), regenerate their livers completely after partial hepatectomy and dogs with Eck fistulae(2) do not. The ability of systemic venous blood to support liver regeneration has been demonstrated. The likelihood of the existence of a portal factor is thereby decreased but not excluded. The requirement of the dog's liver for venous blood in adequate quantity is nevertheless considered established. This is consistent with the observation that the portal vein supplies the liver in dogs with at least 70% of its total blood supply(3).

Summary. 1. Partial hepatectomy has been carried out in dogs with portacaval transposition, with normal hepatic blood supply, and with end to side portacaval shunts. 2. In dogs with portacaval transposition the hepatic venograms showed striking regeneration. 3. Percentile regeneration was somewhat less in these dogs than in the normal but greater than in the dogs with end to side portacaval shunts. 4. These data discount the importance of portal blood *per se* in regeneration of the liver and lend support to the concept that the failure of hepatic regeneration in dogs with Eck fistulae is due in part at least to lack of venous blood flow.

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