mammalian liver, that added insulin causes a breakdown of glycogen. The glycogenolytic properties of insulin have also been observed by Brugsch,[12] Nitzescu[13] and Gigon and Staub.[14] Macleod[15] believes that glycogenolysis is the most important single factor in restoring the blood sugar during the hypoglycemic state. Our experiments, by the direct introduction of insulin into the portal circulation, lend further confirmatory evidence to the conception that insulin in contact with liver cells, is an active glycogenolytic principle.

Conclusion: A transient hyperglycemia follows the portal injection of insulin.

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The Source of Fibrinogen.

P. D. MC MASTER AND D. R. DRURY.

From the Laboratories of The Rockefeller Institute for Medical Research.

The formation of fibrinogen has been ascribed to many tissues and organs of the body. Whipple,[1] Goodpasture[2] and others suggested that this substance takes its origin from the liver and intestinal tract; and recently Foster and Whipple[3] have presented excellent evidence that the liver is the main if not the sole source of fibrinogen. Schultz, Nicholes and Schaefer[4] have produced corroboratory data. Final proof in the matter has waited, however, upon the findings in liverless animals.

In 4 hepatectomized rabbits[5] we have determined the concentration of blood fibrinogen before operation and at various periods thereafter. A postoperative decrease in the substance was always

[12] Brugsch, T., Benatti, A., Horsters, H., and Katz, R., *Biochem. Z.*, 1924, cxlvii, 117.

[13] Nitzescu, L. I., and Popescu-Inotesti, C., *Compt. Rend. Soc. Biol.*, 1923, lxxxix, 1403.

[14] Gigon, A., and Staub, *Klin. Woch.*, 1923, ii, 1670.

[15] Macleod, J. J. R., "Carbohydrate Metabolism and Insulin," Longmans, Green and Co., 1926, 171.

[1] Whipple, G. H., *Am. J. Physiol.*, 1914, xxxiii, 50.

[2] Goodpasture, E. W., *Am. J. Physiol.*, 1914, xxxiii, 70.

[3] Foster, D. P., and Whipple, G. H., *Am. J. Physiol.*, 1922, lviii, 407.

[4] Schultz, E. W., Nicholes, J. K., and Shaefer, J. H., *Am. J. Path.*, 1925, i, 101.

[5] Drury, D. R., *J. Exp. Med.*, 1929, in press.

found. In 6 others a partial depletion of fibrinogen was accomplished after hepatectomy and its concentration in the blood was followed until death. Controls subjected only to defibrination were also studied.

The initial defibrination was accomplished under ether anesthesia by slowly injecting into the jugular vein 100-150 cc. of compatible defibrinated blood while removing an identical quantity from the carotid artery. The procedure was repeated 4 or 5 times. This reduced the blood fibrin concentration to one third to one fifth its original amount. By continuing the blood exchange a still greater reduction was sometimes brought about in the controls. Fibrinogen was estimated in the form of fibrin by the method of Foster and Whipple[6] as modified by Schultz, Nicholes and Schaefer.[4]

In the controls fibrinogen regeneration was exceedingly rapid. Within 5 or 6 hours after a 90% reduction, a complete return to the previous amount was observed, regeneration far more rapid than has been reported for the dog.[7] Twenty-four hours later the concentration had reached a level 50% above the normal figure and in two instances it had doubled within 48 hours.

The findings were wholly different in the liverless rabbit. In 6 animals blood fibrin determinations were made immediately after the hepatectomy and then the partial defibrination was carried out, reducing the circulating amount by 65 to 80%. Four or 5 hours later a slight rise, about 10%, was usually but not always found, indicating the existence of a small reserve within the tissues. Thereafter, however, a marked and progressive decrease from the previous very low figures was invariably observed. Blood specimens taken 9 to 18 hours later showed 38 to 74% reduction in blood fibrin. No changes in the blood hematocrits were found to account for either alteration.

In the hepatectomized rabbits in which no defibrination was attempted there was a similar marked progressive decrease in blood fibrin. In 4 instances the blood fibrin concentration had fallen, 24 hours after hepatectomy, to 35-45% of its preoperative level.

The findings prove that fibrin regeneration does not occur in the absence of the liver.

[6] Foster, D. P., and Whipple, G. H., *Am. J. Physiol.*, 1922, lviii, 365.

[7] Foster, D. P., and Whipple, G. H., *Am. J. Physiol.*, 1922, lviii, 393.