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The stimulating influence of alkali on hepatic glycogenesis.

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The pronounced influence which acids and alkalies exert on the rate at which glycogenase converts glycogen into reducing sugar has suggested the possibility that variations in the activity of this enzyme in the liver cells may depend primarily on changes occurring in the reaction (H-ion concentration) of the immediate environment in which the enzyme is acting.[1] Although there are now many facts which indicate that a condition of hyperglycemia (and glycosuria) usually develops when acids gain entry to the blood and that the opposite condition of hypoglycemia is readily induced with alkalies, yet there is no direct evidence that these changes in the reducing power of the blood are immediately dependent upon corresponding alterations in the rate of hepatic glycogenolysis in warm blooded animals.

A direct method for testing the influence of changes in reaction in the liver cells on the glycogenolytic process is offered in the experimental procedure which has recently been described by Pearce and Macleod.[2] Briefly, this consists in an estimation of the reducing power of the blood removed at short intervals (2–3 minutes) from the portal vein and vena cava inferior (opposite the entry of the hepatic veins), several consecutive estimations being made before, during and after the injection of a dextrose solution under constant pressure, into a branch of the mesenteric vein. When the percentage reducing power is equal in the two bloods, the glycogenolytic process in the liver is presumably dormant; when the percentage is higher in the vena cava than in the portal vein, glycogenolysis must be active; and when lower,

[1] Cf. Pavy and Bywaters, *Journ. Physiol.*, 1910, LXI, p. 168; Elias, *Biochem. Ztschr.*, 1913, XLVIII, p. 120; Elias and Kolb, ibid., 1913, LII, p. 331; Macleod, "Diabetes, etc.," 1913, p. 150; Murlin and Kramer, *Jour. Biol. Chem.*, 1913, XV, p. 365; and *Proc. Soc. Biol. Chem.*, 1915, III, p. 25, and Kramer and Marker, ibid., p. 24.

[2] Macleod and Pearce, *Am. Journ. Physiol.*, 1915, XXXVIII, p. 425.

the opposite (namely, a building up of glycogen out of the injected sugar) must be taking place. In previous investigations, in which neutral solutions were employed, no retention of dextrose by the liver could be demonstrated when about 0.5 gm. was injected into the portal circulation during five minutes.

In the present investigation, the injected dextrose solution was either faintly acid or strongly alkaline, the latter reaction being obtained by adding from 5 to 20 gm. Na_2CO_3 (anhydrous) to 120 c.c. of the solution. At the rates of injection employed, a distinct change occurred in the H-ion concentration of the blood of the portal vein, but much less so in that of the vena cava, as judged by the dialysis-colorimetric method of Levy, Rowntree and Marriott.

In most of the experiments the reducing power of the blood was determined by the method of Lewis and Benedict as modified by R. G. Pearce. In two experiments the Bertrand method was employed after precipitation of the proteins by colloidal iron. The following table depicts some of the most typical results.

TABLE

AVERAGE PER CENT. REDUCING POWER OF BLOOD

No.	Before Injection.		During Injection.		Amount of Dextrose Injected in 5 Minutes.
	In Portal Vein.	In Vena Cava.	In Portal Vein.	In Vena Cava.	
19	0.070	0.068	0.153	0.104	1.6 gm.
20	0.067	0.072	0.098	0.086	1.35 "
25	0.101	0.102	0.190	0.129	0.51 "
32	0.086	0.088	0.208	0.127	0.50 "
27	——	0.126	0.209	0.158	0.48 "
30	——	0.125	0.196	0.100	0.36 "

In Experiments 19, 20, 25, and 31 the picric acid method was employed, and in 27 and 30 that of Bertrand.

Control experiments in which the dextrose solution was made faintly acid, or contained an excess of sodium chloride (16 per cent.) did not reveal any such difference in the reducing power of the two bloods. Neither did injections of acid or alkali alone cause any difference. Many other details remain to be further investigated. For the present, however, the results clearly demonstrate that, when dextrose is injected in moderate amounts into the

blood of the portal system, a large proportion of it becomes retained in the liver provided alkali is simultaneously injected in sufficient amount to produce a distinct lowering of the H-ion concentration of the portal blood. A similar retention can not be demonstrated by the above method when the dextrose solution is neutral or acid, or when it is made markedly hypertonic with sodium chloride.

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Endothelial opsonins.

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If the blood-free liver of a normal rabbit is repeatedly perfused with a sample of Ringer's solution containing a known number of pneumococci, no diminution in the pneumococcic count of the perfusion fluid is observed, even after a dozen passages through the liver.

If the liver of an actively immunized rabbit is similarly perfused, the pneumococcic count is rapidly decreased. After three or four passages, the perfusion fluid usually becomes sterile.

Histological study of the perfused liver now shows numerous pneumococci adherent to the capillary endothelium. Few if any agglutinated masses are seen.

Normal rabbit serum added to the perfusion fluid in amounts not exceeding 10 per cent. causes no appreciable retention of the pneumococci by normal livers. Immune serum similarly added causes a quantitive retention of the pneumoccoci.

Immune serum will cause this retention when tested in less than a hundredth of the concentration necessary to cause agglutination.

The serum component causing the pneumococcic retention is thermo-stable (60° C., 30 min.).

Unagglutinated pneumococci sensitized by exposure to immune serum and then washed free from serum, are retained quantitatively by normal livers.

The serum component responsible for the retention is therefore