trusion of the a. f. cells in the glomerular tuft; hyperplasia of the a. f. cells of the vas afferens followed by glomerular regression; transformation of ordinary smooth muscle cells into a. f. cells: a process which is accompanied by mitotic activity. In chronic cases of eight and seventeen months 'duration all the juxta glomerular apparatuses are hyperplastic and secretion granules appear in the a. f. cells while no qualitative changes occur in the tubules.

Since renal ischemia causes hyperplasia and hypertrophy of the a. f. cells which in the control rabbit have cytologic features of endocrine activity; since carefully graduated ischemia stimulates the a. f. cells at the exclusion of any qualitative changes in the tubules and favors the apparition of secretion granules in the a. f. cells of the dog, normally devoid of them, it must be concluded that the endocrine activity of the a. f. cells is related to the production of the hypertensive substance present in the ischemic kidney. It is suggested that in normal conditions the a. f. cells regulate the tonus of the renal arterioles.

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Effect of Added Glucose on Rate of Appearance of Free Sugar in Liver Brei.

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Previous work has shown that a rise in the blood sugar level in the normal animal causes a compensatory decrease in the sugar output of the liver.[1, 2] The operation of this homeostatic mechanism to maintain the normal blood sugar level depends upon the presence of the equal and opposite influences of insulin and other hormones. But, providing this endocrine balance is normal, no extra insulin need be secreted for each regulatory action.[1] Indeed, the regulation has been demonstrated in the "Houssay animal," in which insulin and the anterior pituitary hormones are entirely lacking.[3] The ab-

[1] Soskin, S., Allweiss, M. D., and Cohn, D. J., *Am. J. Physiol.*, 1934, **109**, 155.

[2] Soskin, S., Essex, H. E., Herrick, J. F., and Mann, F. C., *Am. J. Physiol.*, 1938, **124**, 558.

[3] Soskin, S., Mirsky, I. A., Zimmerman, L. M., and Heller, R. C., *Am. J. Physiol.*, 1936, **114**, 648.

sence of the hormones representing both sides of the endocrine balance does not cause as great a disturbance as when one side is allowed to act unopposed, and results merely in an upward shift of the blood sugar level (threshold) at which regulation occurs.

These results indicated the existence of an intrinsic regulating mechanism in the liver cells, dependent upon the endocrines only for the fine adjustment of its threshold of response. The present work was done with minced liver *in vitro* to confirm the postulated intrinsic hepatic mechanism, by eliminating all extra-hepatic factors.

Livers of normal, fed dogs were used for all experiments. The organ was removed under nembutal anesthesia, and finely minced in a previously cooled meat grinder. Samples weighing approximately 1.5 g were put into Erlenmeyer flasks containing 5 cc of Hastings' phosphate solution.[4] The flasks were oxygenated for 5-10 minutes, and shaken in a water bath at 38°C.

Total carbohydrate and free sugar were estimated by the method of Tsai[5] as modified by Benoy and Elliott,[6] using the Somogyi reagent. Inorganic phosphate was determined by the method of Fiske and Subbarow,[7] as adapted to the photoelectric colorimeter.

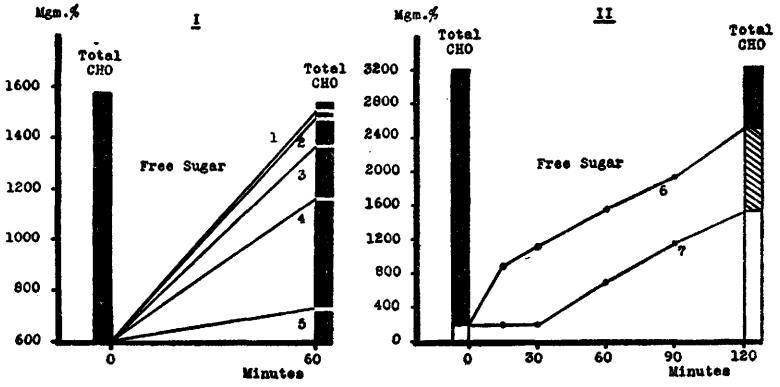

FIG. 1.

I. The influence of different amounts of glucose added to each vessel, upon the appearance of free sugar in liver brei in 1 hour. 1. No addition. 2. 5 mg glucose added. 3. 10 mg added. 4. 20 mg added. 5. 40 mg added.

II. A comparison of the rates of appearance of free sugar at different time intervals, with and without the addition of glucose to liver brei. 6. No addition. 7. 20 mg glucose added.

The blocks representing total carbohydrate determinations at the beginning and end of each experiment, indicate that there was no significant loss of carbohydrate from the system.

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5 Tsai, L., *Chinese J. Physiol.*, 1933, **1**, 91.

6 Benoy, M. P., and Elliott, K. A. C., *Biochem. J.*, 1937, **31**, 1268.

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TABLE I.

Inhibition, by added glucose, of appearance of free Sugar in mg per 100 g of Liver, in 60 Minutes.

Amt of dextrose added mg %	Exp. No. 1			Exp. No. 2			Exp. No. 3		
	Free sugar			Free sugar			Free sugar		
	Min 0	Min 60	% Inhib.	Min. 0	Min. 60	% Inhib.	Min. 0	Min. 60	% Inhib.
0	254	1997	—	184	745	—	172	301	—
100	”	2027	0	”	567	24	”	224	25
200	”	1565	22	”	585	22	”	174	42
400	”	1229	38	”	330	55	”	151	50
800	”	1260	37	”	316	58	”	208	31
1600	”	958	52	”	376	50	”	—	—
Total CHO	3313	3578	—	1234	1209	—	404	401	—

Representative results are shown in Fig. 1 and Table I. It can be seen from these data that the addition of dextrose at the beginning of the incubation period inhibits the rate of appearance of free sugar for ½-1 hour, after which the rate of appearance of free sugar begins to approximate that of the control (without added sugar). The degree of inhibition is, within certain ranges, proportional to the amount of sugar added. If certain sugar concentrations are exceeded the degree of inhibition becomes smaller.

It is at present not possible to define clearly the mechanism of this inhibition. But sufficient data are at hand, in the literature on glycogenolysis to suggest certain conclusions. Thus the work of Schäffner,[8, 9] Cori,[10, 11, 12] Kiessling[13] and Lehmann[14] demonstrates that the first steps in glycogenolysis are: the phosphorylosis to glucose-l-monophosphate, conversion to the 6-ester and further transformation to fructose diphosphate. Glucose has been shown to inhibit the first step in this chain.[14, 15]

Summary and Conclusions. It is concluded that the inhibition of the rate of appearance of free sugar in glycogenolyzing liver brei, probably depends upon an inhibition of the first step in glycogenolysis, namely, the phosphorylosis of glycogen to glucose-l-monophosphate. These results confirm the previously postulated intrinsic hepatic homeostatic mechanism which contributes to blood sugar regulation by determining the rate of sugar output by the liver. Since it occurs *in vitro,* the non-essential nature of extra insulin secretion for this regulatory activity is confirmed.[3] The actual relationship of insulin and other hormones to this mechanism has already been indicated.

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13 Kiessling, M., *Naturwiss.*, 1939, **27**, 129.

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