Absence of Hyperglycemic Effect of Glucagon in the Eviscerate Rat.* (20600)

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In these experiments, glucagon (a hyperglycemic principle occurring in extracts of pancreas) caused hyperglycemia in normal but not in eviscerated rats.

Methods. General details have been published(1,2). Male rats were eviscerated at 250 ± 2 g weight. All rats were studied under barbiturate anesthesia. The eviscerated rats were given solutions of glucose with and without insulin and antibiotics by continuous intravenous injection at the rate of 20 ml per 24 hours per rat. The normal rats received equal volumes of physiological saline. The glucose load is expressed as mg of glucose per 100 g of rat per hour (mg/100 g/h). When insulin (regular) was added, it was given at the rate of 4 units per 24 hours per rat. The antibiotic dosage was 10,000 units of penicillin and 5 mg of streptomycin per rat per 24 hours. A highly purified(3) preparation of glucagon was added to the glucose solution in some experiments, but in others, each dose was contained in 0.1 ml of physiological saline which was injected rapidly into the saphenous vein of the left hind leg. Glucose was determined (4) on tail blood. The temperature was 26.5 ± 0.5°C.

Experiments and results. In Exp. 1 the eviscerated rats received a glucose load of 64/100 g/h with insulin and the normal rats received only saline by continuous intravenous injection for periods of 90 minutes. Each rat received a separate injection of glucagon 30 minutes after the continuous injections were started. All doses of glucagon caused hyperglycemia in the normal rats but did not significantly affect the level of blood glucose in the eviscerated rats. The data are in Table I.

In Exp. 2 (Fig. 1) glucagon was given in the infusion fluid at a dose of 25 μg per rat per hour and an added dose of 25 μg contained in 0.1 ml of physiological saline was given separately at the time the continuous injections were started. Six pairs of eviscerated rats were given a glucose load of 64/100 g/h plus insulin for a period of 2 hours follow-

TABLE I. Effect of Glucagon upon Level of Blood Glucose in Eviscerate and Non-Eviscerate Rats. Insulin and glucose (64/100 g/h) to eviscerate rats. Glucagon administered separately. Individual values, mg %.

Dose μg glucagon	Non-eviscerate					Eviscerate				
		Min. post-injection					Min. post-injection			
	Initial	15	30	45	60	Initial	15	30	45	60
1	121	153	156							
10	126	153	195							
	127	142	186							
10	99	151	164	165	163	117	117	109	118	116
	102	147	186	181	174	120	118	87	123	118
	111	165	162	168	166	102	91	93	87	93
	108	153	165	183	181	138	145	148	159	165
	111	141	162	168	162	117	121	123	118	106
	108	144	172	162	138	96	75	69	69	66
25	115	177	192	186	156	117	99	106	111	120
	111	156	198	211	164	129	138	133	133	132
100	132	172	181	219	228	127	103	124	120	102
	126	187	189	207	192	129	133	135	165	168
250	120	171	199	216	213	96	103	85	87	90
	123	154	189	231	216	123	121	130	135	138

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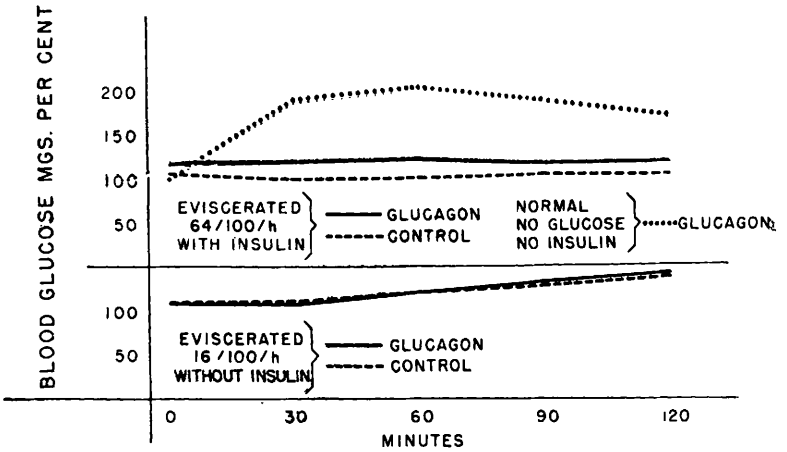

FIG. 1. Absence of hyperglycemic effect of glucagon in eviscerated rat; presence of hyperglycemic effect of glucagon in normal rat. Avg of 6 rats/group. Blood glucose determined at intervals of 30 min.

ing evisceration. Six pairs of eviscerated rats were given a glucose load of 16/100 g/h without insulin for 2 hours. One rat of each pair received glucagon whilst the other rat of each pair received added saline only. Six normal rats were given continuous intravenous injections of saline without glucose or insulin. The normal rats developed hyperglycemia following the injection of glucagon but the blood glucose of the eviscerated rats did not rise above that of their controls.

In Exp. 3, 19 pairs of eviscerated rats were each given a glucose load of 40/100 g/h with insulin and antibiotics for 24 hours. One rat of each pair received 500 μg of glucagon per 24 hours added to the infusion fluid. At the end of the 24 hours, the rats given glucagon had an average level of blood glucose of 105 $\pm$ 24 and the control rats, an average of 112 $\pm$ 8.5.

In order to test the stability of glucagon, a solution of 10 mg in 100 ml was kept at room temperature for 24 hours and then administered by continuous intravenous injection to 4 normal rats under barbiturate anesthesia for a period of 30 minutes. Each rat received 10 μg of glucagon. Hyperglycemia developed in each animal, the average value for blood glucose being 109 mg % at the beginning of injection and 183 mg % at the end of 30 minutes.

Discussion. It has been shown that hepatic glycogenolysis occurs following the injection of glucagon(5). The data of the present study fail to show any extra-hepatic effect of glucagon upon the tolerance of the rat for intravenously administered glucose but these observations do not exclude the possibility that glucagon has extra-hepatic effects upon metabolism.

Summary. Eviscerated rats were given continuous intravenous injections of glucose. The intravenous injection of glucagon failed to affect the level of blood glucose in eviscerated rats but did cause hyperglycemia in normal rats.

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