v191, 807.
5. Olitsky, P. K., and Tal, C., PROC. SOC. EXP. BIOL. AND MED., 1952, v79, 50.
6. Webster, L. T., *J. Exp. Med.*, 1933, v57, 793.
7. Wolf, A., Kabat, E. A., and Bezer, A. E., *J. Neuropath. and Exp. Neurol.*, 1947, v6, 333.
8. Ferraro, A., and Cazzullo, C. L., *ibid.*, 1948, v7, 235.
9. Pratt, R. T. C., Compston, N. D., and McAlpine, D., *Brain*, 1951, v74, 191.

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Effect of Continuous Injection of Glucagon upon Glycosuria of Partially Depancreatized Rats. (20907)

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Glucagon is a hyperglycemic principle occurring in extracts of pancreas. In the present study the continuous intravenous injection of glucagon caused a temporary increase in the urinary glucose of the mildly diabetic rat.

Methods. Male rats of the Sprague-Dawley strain were maintained on Archer Dog Pellets until they were partially depancreatized at a weight of 275 to 280 g. After reaching a weight of 300 g they were force-fed a medium carbohydrate diet(1) by stomach tube each morning (8:30 to 9:00 a.m.) and afternoon (4:15 to 5:00 p.m.) Each rat was placed in a metabolism cage which restricted its activity so that the animal was unable to reverse its position. Each 24-hour dose of highly purified glucagon(2) was contained in one ml of physiological saline and was administered continuously by either intra-jugular or subcutaneous injection. A fresh solution was prepared every 24 hours.

It was found to retain its glycogenolytic potency during the period of administration. Saline only was injected during the control periods. Attempts to preserve asepsis were not uniformly successful. Infection of the vein at the site of the indwelling needle was found in about 40% of the animals at autopsy. The data of this report represent only those animals in which intravenous infusion was successfully maintained throughout the experiment. Urine was collected at the same hour (8:00 to 8:30 a.m.) each day for the quantitative determination of glucose(3).

Experiment. In Exp. 1, six normal rats were given glucagon by continuous subcutaneous injection in doses of 0.05 mg the 1st day, 0.1 the 2nd day, 0.2 the 3rd day, 0.5 the 4th day, and 1.0 mg the 5th day. These rats remained free from glycosuria during the control periods and during the injection of glucagon.

In Exp. 2, six mildly diabetic partially depancreatized rats were given glucagon by continuous subcutaneous injection every other day. Doses of 0.05, 0.1 and 0.2 mg per rat per day were tested with negative results. The experiment was extended on 5 similar animals using doses of 0.05, 0.1, 0.2 and 0.5 mg of glucagon per rat per day with negative results.

In Exp. 3, six mildly diabetic partially depancreatized rats were given glucagon by continuous intra-jugular injection at a dosage of 0.5 mg/rat/day for 8 days. In each rat there was a temporary increase in urinary

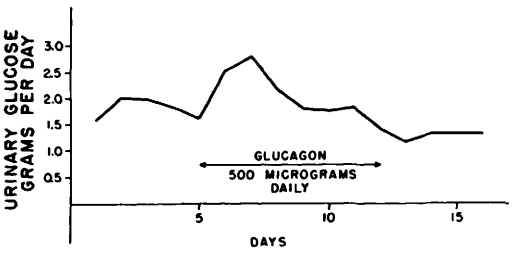

FIG. 1. Effect of continuous intravenous injection of glucagon upon glycosuria of 6 partially depancreatized rats. Average.

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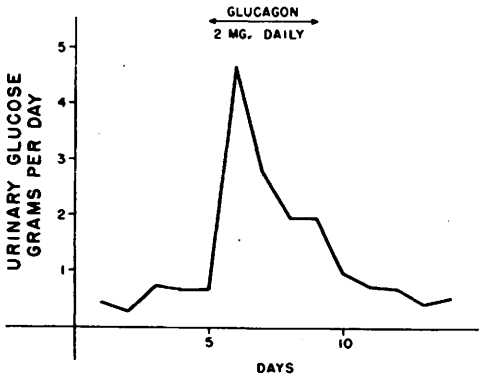

FIG. 2. Effect of continuous intravenous injection of glucagon upon glycosuria of a partially depancreatized rat.

glucose which reached a peak during the 2nd day and then fell to preinjection levels or lower by the 4th day. The data are in Fig. 1. Similar individual rats were given glucagon in doses of 0.1 to 2 mg/rat/day for 5 days. Each rat showed exacerbation of the glycosuria which reached a peak on the 2nd day and then abated. The response of one animal is shown in Fig. 2.

Discussion. Glucagon has a positive effect upon the glycosuria of the partially depancreatized rat. Our data indicate that the exacerbation of diabetes is temporary but definite conclusions may not be warranted. Some veins were found to be infected at autopsy although it was demonstrated that the infusion fluid still entered the blood in those animals which are reported here. There is evidence that the pancreas secretes a hyperglycemic agent(4) which may or may not be identical with glucagon. At this time the origin of glucagon, its hormonal nature and its role in body economy have not been clearly established.

Summary. When a highly purified preparation of glucagon was administered to partially depancreatized, force-fed rats by continuous intravenous injection there was temporary exacerbation of the diabetes. The continuous subcutaneous injections of glucagon to normal and to partially depancreatized rats were ineffective in the doses (0.05 to 1 mg/rat/day) tested.

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1. Ingle, D. J., Beary, D. F., and Purmalis, A., *Endocrinology*, 1953, v52, 403.

2. Staub, A., Sinn, L., and Behrens, O. K., *Science*, 1953, v117, 628.

3. Shaffer, P. A., and Williams, R. D., *J. Biol. Chem.*, 1935, v111, 707.

4. Foa, P. P., Magid, E. B., Glassman, M. D., and Weinstein, H. R., PROC. SOC. EXP. BIOL. AND MED., 1953, v83, 758.

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Eosinophils of Blood During Prolonged Exposure to Cold and Chronic Administration of Cortisone Acetate.*† (20908)

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In accordance with the concept of the General-Adaptation-Syndrome, it has been postulated that an increased secretion of adreno-cortical steroids occurred when an animal was placed under prolonged exposure to stress(1). This increased release of adrenal corticoids has been demonstrated indirectly by changes in the concentration of different metabolites in the blood during the period of exposure(1). The use of the adrenal ascorbic acid or adrenal cholesterol depletion tests as indices of adrenal activity have also revealed an immediate and marked release of adreno-corticoids(2). However, both substances returned to normal or above normal during prolonged exposure to cold(3). Similarly, prolonged exposure to a low atmospheric

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