50 to 70 milli-units per k body weight. As demonstrated by Sayers(4), the ascorbic acid response in the rat reaches a maximum at about 20-30 minutes after ACTH injection.

In evaluating the data in this series it is important to bear in mind that all the adrenals included in this series were from patients with relatively advanced carcinomata and no comparable data are as yet at hand from human adrenals of noncancerous patients.

Summary. 1. The mean ascorbic acid content of the adrenal cortex of human cancer patients prior to ACTH treatment was found to be 131 ± 8 mg per 100 g tissue in the male and 139 ± 5 mg % in the female. 2. A 32% depletion in cortical ascorbic acid was found at 2 to 3 hours after intravenous injection of 25 U.S.P. units of ACTH. 3. The dosage of ACTH required to produce this depletion appears to be about 7 to 8 times that required per kg of body weight for the male hypophysectomized rat and the time elapsed between ACTH injection and maximal ascorbic depletion appears to be greater than 3 hours in the human.

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Effect of Continuous Injection of Epinephrine upon the Glycosuria of Partially Depancreatized Rats. (20558)

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In acute experiments on intact animals, epinephrine causes hyperglycemia, redistribution of glycogen stores and occasionally a mild glycosuria of short duration. The effects of the prolonged injection of epinephrine are less well studied. Epinephrine was administered continuously to normal and to partially depancreatized rats for periods of 3 and 4 weeks. Increased amounts of glucose were excreted during the injection of epinephrine.

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. Depancreatized rats and unoperated rats were thereafter force-fed a medium carbohydrate diet(1) by stomach tube each morning (8:30 a.m.) and afternoon (4:15 to 5:00 p.m.). Each 24-hour dose of epinephrine hydrochloride (Upjohn) was contained in 1 ml of physiological saline with 1 mg of ascorbic acid added as an antioxidant. The control rats received an equal amount of saline and ascorbic acid. Each rat was placed in a metabolism cage which restricted its activity so that the animal was unable to reverse its position. A 21-gauge needle, having a small barb attached to its shank to prevent its withdrawal, was placed subcutaneously. Sterile needles were used for replacement every 48 hours. The solutions were administered to 6 rats simultaneously by a continuous injection machine. Three of the 6 rats received epinephrine and 3 received control injections. The room temperature was 74° to 78°F. Urine was collected at the same hour (8:00 to 8:30 a.m.) each day for the quantitative determination of glucose(2).

Experiments and results. Exp. 1 (Fig. 1)

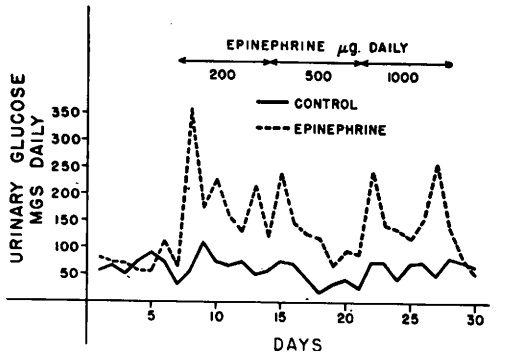

FIG. 1. Urinary glucose of normal rats with and without epinephrine. Avg for 6 rats/group.

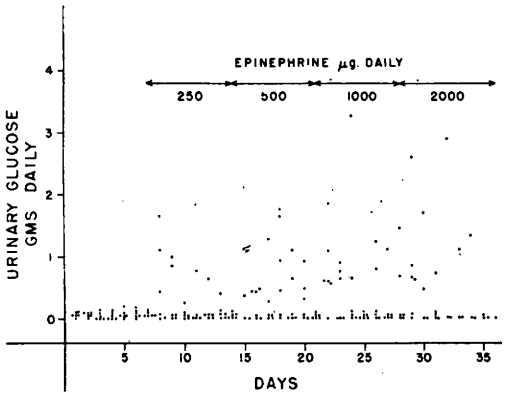

FIG. 2. Effect of epinephrine upon urinary glucose of 6 partially depancreatized rats without spontaneous glycosuria. Individual values.

involved 12 normal rats. Following a control period of 7 days, each of 6 rats received daily 200 μg of epinephrine for 7 days, 500 μg for 7 days and 1000 μg for 7 days, followed by a second control period for 7 days. The 6 control rats simultaneously received 1 ml of saline per rat daily for 21 days. All of the rats excreted small amounts of reducing substances during the control periods. During the injection of epinephrine there was a sharp but small rise in the excretion of reducing substances which tended to abate during the continued administration of that dose until the increase in dosage caused a small and temporary rise. When the injection of epinephrine was stopped, the excretion of reducing substances fell to control levels.

Exp. 2 (Fig. 2) involved 6 partially depancreatized rats which did not excrete more than 100 mg of reducing substances per rat per day during the control periods. Epinephrine was administered in doses per rat per day of 250, 500, 1000, and 2000 μg for 7 days per dose. Each rat excreted significant amounts of glucose on several days during the injection of epinephrine. The glycosuria tended to occur within 24 to 48 hours after the beginning of injections or upon an increase in dosage. Four of the rats died during the administration of 2000 μg of epinephrine daily.

Exp. 3 (Fig. 3) involved 18 mildly diabetic rats. Following an initial control period of 7 days, each of 9 rats received daily 200 μg of epinephrine for 7 days, 500 μg for 7 days and 1000 μg for 7 days. There followed a second control period of 7 days. The 9 control rats each received 1 ml of saline daily during the 21-day injection period. During the injection of 200 μg of epinephrine per rat per day there was a temporary increase in glycosuria, there was a slight rise when the dose was increased to 500 μg daily and a more striking but temporary rise when the dose was increased to 1000 μg daily. When the injections were stopped, the glycosuria decreased to values similar to those of the control animals which had shown a gradual decrease in glycosuria.

Discussion. In acute experiments epinephrine stimulates hepatic glycogenolysis. This is not the only effect of epinephrine upon carbohydrate metabolism for it inhibits glucose tolerance in the liverless rat(3), and there is other evidence(4) that it affects the peripheral distribution and utilization of carbohydrate. In partially depancreatized rats, epinephrine can cause the excretion of more glucose than

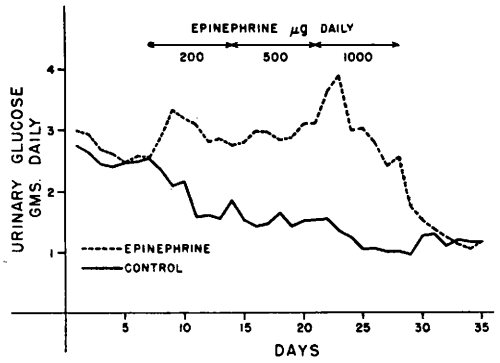

FIG. 3. Urinary glucose of mildly diabetic rats with and without epinephrine. Avg for 9 rats per group.

is present in liver at any one time. Rats without spontaneous glycosuria (Exp. 2, Fig. 2) excreted up to 3 g of glucose during a 24-hour period. If this temporary exacerbation of diabetes is due to an effect of epinephrine upon liver, it must be described in terms of changes in turn-over rather than as a single discharge of glucose from liver. The maximum glycosuria usually occurred on the 2nd day after beginning the continuous injection of epinephrine.

The possibility that epinephrine stimulates the adrenal cortices to secrete diabetogenic amounts of cortical hormones can be considered. Large doses of epinephrine can stimulate the adrenal cortices via the increased release of corticotropin in acute experiments(5), but there is no satisfactory evidence known to the authors that a true state of hypercorticalism can be induced by epinephrine.

The largest dose of epinephrine used in this study, 1000 μg per day, is near the maximum that can be tolerated by the rat. When the dose was doubled, as in Exp. 2, some of the rats died. In preliminary studies it was found that either a dose of 500 or 1000 μg of epinephrine per rat per day would cause death in some animals unless the animals were first adapted to a smaller dose.

Summary. Epinephrine was administered to normal and to partially depancreatized force-fed rats by continuous subcutaneous injection for periods of 3 and 4 weeks. Simultaneously the control animals were injected with saline. Increased amounts of glucose were excreted by both normal and partially depancreatized rats during the injection of epinephrine. The peak response occurred on the second day after starting the injection of epinephrine or increasing the dose. All of the animals showed adaptation to epinephrine so that the peak response was not sustained.

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Enzymatic Evidence for Intrinsic Oxytocic Activity of the Pressor-Antidiuretic Hormone. (20559)

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Until recently there has been uncertainty as to whether the oxytocic activity of vasopressin preparations was due to contamination of the preparations with oxytocin or to an intrinsic oxytocic activity of the pressor-antidiuretic hormone. Evidence for the latter explanation was afforded by the work of Popenoe, Pierce, du Vigneaud, and van Dyke (1). They found that the most highly purified arginine-vasopressin prepared in this laboratory possessed approximately 600 pressor units per mg by the arterial blood pressure method in cats and an oxytocic activity of 80-90 units per mg by the method of Coon(2), based on the lowering of the blood pressure of the fowl, and 30 units per mg by the rat uterus method.† On the other hand, a highly purified oxytocin preparation(3) possessing

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† Coon(2) found that when the pressor-oxytocic ratio of a pituitary solution was above 2.5 the oxytocic assay value obtained by the depressor method was higher than that obtained by the guinea pig uterine method.