

onate concurrently. The possibility that the antagonism in the mammae is due to pituitary suppression resulting in mammary gland "stunting" seems to be ruled out in our experiment in which relatively small doses of estrogen and the androgen from functioning testes were employed.

**Conclusion.** Castrate male mice of the F<sub>1</sub> hybrid generation between the A and Z stocks bearing subcutaneous ovarian grafts developed mammary cancer more readily than do virgin female mice of this cross. Only 1 of 39 non-castrate males bearing ovarian grafts de-

velop mammary carcinoma as little mammary development occurred. Additional experiments seemed to indicate that the ovaries in the non-castrate male mice were producing an appreciable amount of estrogen although measurably less than those carried in castrate males. There appeared, also, to be an antagonism between estrogens and androgens as far as stimulation of the vaginal and mammary epithelium is concerned. Granulosa cell tumors occasionally occurred in ovarian grafts of old male and female mice of this hybrid cross.

## 16708 P

### The Effect of 11-Desoxycorticosterone Acetate Upon the Glycosuria of Partially Depancreatized Rats.

DWIGHT J. INGLE.

*From the Research Laboratories, The Upjohn Company, Kalamazoo, Mich.*

This study shows that large doses of 11-desoxycorticosterone acetate cause an exacerbation of the diabetes of partially depancreatized, force-fed rats.

**Methods.** Male rats of the Sprague-Dawley strain were maintained on Archer Dog Pellets until they reached a weight of 300 g. Ten rats were depancreatized by the method of Ingle and Griffith.<sup>1</sup> After diabetes was established all of the animals were placed in

metabolism cages and were fed a medium carbohydrate diet made according to Table I. All of the animals were force-fed by stomach tube each morning (8:30 to 9:15 A.M.) and afternoon (4:15 to 5:00 P. M.). The techniques and diets were modifications of those described by Reinecke, Ball and Samuels.<sup>2</sup> During the period of adaptation to force feeding, the amount of diet was increased gradually to prevent "food shock." A full feeding of 26 cc of diet per rat per day was reached on the 5th day.

The animals were kept at a temperature of 74° to 78°F and a humidity of 30 to 35% of saturation. Twenty-four-hour samples of urine were collected at the same hour (8:00 to 8:30 A.M.) and were preserved with thymol. Urine glucose was determined by the method of Benedict.<sup>3</sup>

The 11-desoxycorticosterone acetate (Cortate, Schering) was made up in sesame oil at 5 mg per cc. It was given by subcutaneous in-

TABLE I.  
Medium Carbohydrate Diet.

| Constituent                             | G       |
|-----------------------------------------|---------|
| Cellu flour (Chicago Dietetic Supply)   | 120     |
| Osborne & Mendel salt mixture           | 40      |
| Dried yeast (Pabst)                     | 100     |
| Wheat germ oil                          | 10      |
| Cod liver oil                           | 10      |
| Vitamin K (2-methyl-1,4-naphthoquinone) | 100 mg  |
| Mazola oil                              | 200     |
| Casein (Labco)                          | 160     |
| Starch                                  | 200     |
| Dextrin                                 | 190     |
| Sucrose                                 | 200     |
| Water to make total of                  | 2000 cc |

<sup>1</sup> Ingle, D. J., and Griffith, J. Q., Chapter 16, *The Rat in Laboratory Investigation*, J. B. Lippincott Co., Philadelphia, 1942.

<sup>2</sup> Reinecke, R. M., Ball, H. A., and Samuels, L. T., *Proc. Soc. Exp. Biol. and Med.*, 1939, **41**, 44.

<sup>3</sup> Benedict, S. R., *J.A.M.A.*, 1911, **57**, 1193.

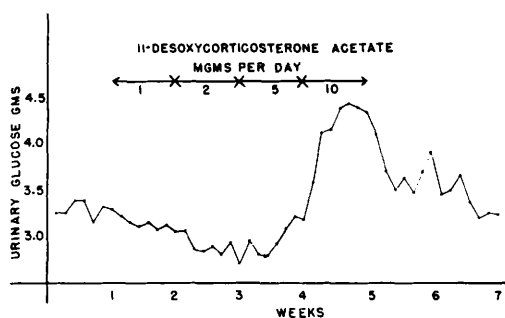


FIG. 1.

Effect of 11-desoxycorticosterone acetate upon the average level of urinary glucose for 10 partially depancreatized rats.

jection in divided doses each morning and late afternoon.

**Experiments and results.** Ten mildly diabetic rats were observed for periods of several weeks prior to the beginning of the experiment. All of the rats received doses of 1, 2, 5 and 10 mg of 11-desoxycorticosterone acetate for periods of 7 days per dose. At the completion of the injection periods the rats were observed during an additional control period of 14 days before the experiment was terminated. Several days elapsed between the beginning of the injection period for each rat and those tested subsequently so that possible unknown variables related to time were less likely to cause fortuitous shifts in the average level of glycosuria. This is an important control for on many occasions we have observed small but significant spontaneous shifts in the level of glycosuria in most or all of a series of diabetic animals under rigid experimental conditions and constant food intake. The results are shown in Fig. 1. During the admin-

istration of 1 and 2 mg of the steroid per day there was an average decrease in the level of urinary glucose representing a change in 7 of the 10 experimental animals. When 10 mg per day of 11-desoxycorticosterone acetate were given, there was an exacerbation of the glycosuria in each of the 10 rats which decreased to pre-injection levels following the withdrawal of the hormone.

**Discussion.** The decrease in glycosuria which occurred in most of the rats during the administration of 1 and 2 mg per day of the steroid may have been due to the compensatory suppression of the secretion of the 11-oxy steroids by the adrenal cortices according to the hypothesis of Selye and Dosne.<sup>4</sup> However, the changes were not sufficiently striking to permit the definite conclusion that the decrease was caused by the administration of the steroid. The exacerbation of glycosuria during the injection of 10 mg per day of the steroid was clearly significant and supports the conclusion that 11-desoxycorticosterone does affect carbohydrate metabolism when given in large doses.

**Summary.** Ten mildly diabetic force-fed rats showed an average decrease in the level of urinary glucose during the administration of 1 and 2 mg of 11-desoxycorticosterone acetate per day. When the dosage was increased to 10 mg of the steroid per day the glycosuria was exacerbated in all of the animals and decreased to the pre-injection level when the administration of the steroid was stopped.

<sup>4</sup> Selye, H., and Dosne, C., *Endocrinology*, 1942, **30**, 581.