

Diuretic Effect of Progesterone.*

HANS SELYE AND LUCY BASSETT.

From the Department of Anatomy, McGill University, Montreal, Canada.

In the course of various experiments in which progesterone had been administered to normal and hypophysectomized rats we observed that this compound greatly increases urine output. We felt that an action of the corpus luteum hormone on diuresis may perhaps throw some light on the cause of the changes in water metabolism observed during normal and pathological pregnancies. Therefore this effect has been subjected to a quantitative analysis in normal and hypophysectomized rats whose urine was collected daily in metabolism cages.

Twenty-four albino females with an average weight of 105 g have been divided into 4 groups of 6. Group I was hypophysectomized and then given daily subcutaneous injections of 10 mg of progesterone in 0.4 cc of peanut oil. Group II was hypophysectomized and given daily subcutaneous injections of 0.4 cc of peanut oil only. Groups III and IV remained intact but received the same injections as Groups I and II respectively. Since hypophysectomy in itself is usually accompanied by a transitory marked diuresis and since the animals need some time to become used to life in individual metabolism cages and daily injections, we did not collect the urine during the first fortnight. After this however, accurate measurements of water intake and output were made on every animal during the 6 subsequent days. Table I shows the urine output during one day. For the sake of brevity the values obtained on other days are omitted since they were essentially the same as those

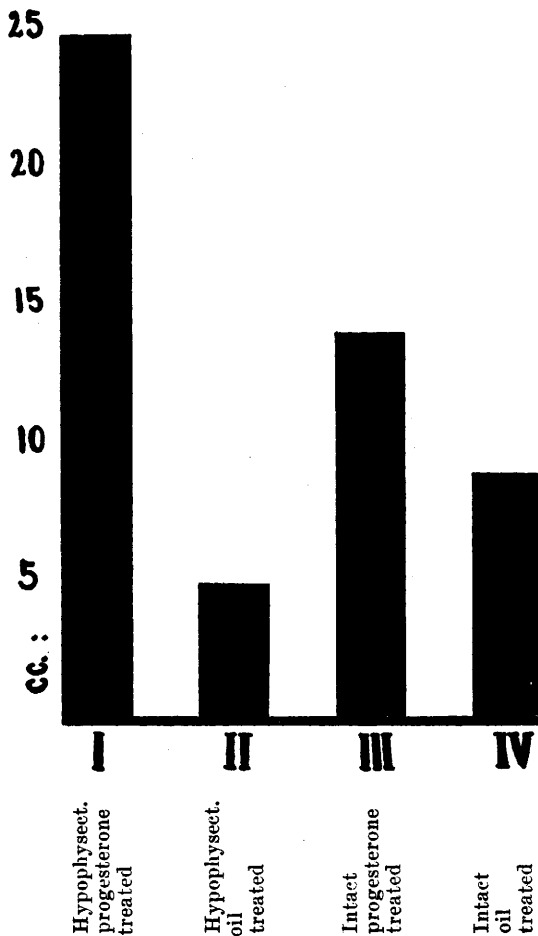
TABLE I.
24-hour Urine Excretion Under the Influence of Progesterone in Normal and Hypophysectomized Rats Expressed in cc.

Rat No.	1	2	3	4	5	6	Avg
I Hypophysectomized progesterone treated	11	46	12	21	25	22	23
II Hypophysectomized oil treated	0	4	2	5	2	10	4
III Intact progesterone treated	19	16	13	16	15	10	15
IV Intact oil treated	6	11	8	9	9	6	8

* The expenses of this investigation were defrayed by a grant received from the Schering Corporation of Bloomfield, N. J., through the courtesy of Dr. G. Stragnell. The progesterone was kindly supplied by Dr. E. Schwenk of the same Corporation.

given in the Table. A summary of the average daily output throughout the 6-day observation period is given in Graph I.

We believe that our experiment clearly indicates that progesterone increases the urine output both in intact and in hypophysectomized rats. Although the hypophysectomized controls excreted only about half as much urine as the normals, the progesterone-treated hypophysectomized animals voided much more than any other group in our experiment. The urine output of the individual rats varied somewhat from day to day but it was not uncommon for progesterone treated hypophysectomized animals to excrete during 24



GRAPH 1.

Average daily urine output per rat under the influence of progesterone in hypophysectomized and normal animals.

hours an amount of urine corresponding to half their body weight.

Since the water intake was approximately the same as the output we did not deem it necessary to include the values for water intake in our table.

It seemed of some interest to establish whether increased urine output is merely the result of the increased intake. For this purpose 15 cc of tap water was administered by stomach tube to each rat and then water and food were withdrawn from all animals during 24 hours. Here again the progesterone-treated animals excreted the water more rapidly than the oil-treated controls. This was true both in the case of the intact and the hypophysectomized animals. It is of interest however, that 4 out of 6 oil-treated hypophysectomized controls succumbed from water intoxication after the administration of the relatively large amount of 15 cc while no casualties occurred in any other group. This is in accord with many previous observations made in this laboratory which indicate that progesterone increases the general resistance of hypophysectomized rats.

We wish to call attention to the fact that experiments performed by the senior author in coöperation with Miss C. Dosne indicate that desoxycorticosterone acetate exerts a diuretic effect similar to that of progesterone. These latter observations will be published in detail in the near future.

Summary. Progesterone increases the urine output both in normal and in hypophysectomized rats. Although the untreated hypophysectomized animal excretes less than the normal amount of urine, progesterone stimulates water excretion much more markedly in the absence than in the presence of hypophysis. In hypophysectomized rats, it may lead to the excretion of an amount of urine corresponding to 50% of the experimental animal's total body weight; a diuresis reminiscent of diabetes insipidus. The resistance of hypophysectomized animals to water intoxication is increased by progesterone.