

# EFFECTS OF NATURAL AND SEMISYNTHETIC ADRENAL CORTICAL HORMONES ON THE GONADS OF ADULT FEMALE ALBINO RATS

By

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and Domanowsky (6) reported that administration of large dose of corticosterone to adult female rats resulted in hypertrophy and hyperactivity of ovary with marked increase of interstitial tissue. Blumenthal *et al.*, (1) observed that cortisone stimulated restoration of endometrium after castration atrophy. In addition to producing an active proliferation of endometrium cortisone brought about marked squamous change in the cervix. Numerous other investigators concluded from their observations that corticoids adversely affect female sex organs. Lohmeyer and Vasterling (5) studied the influence of prednisone on the structure and function of female sex organs of rats. They reported complete absence of fertility in prednisone treated rats although there were no detectable morphological changes in sex organs. In a similar experiment they have demonstrated adverse effect of cortisone on fertility of female rats. It was further demonstrated that in rats spayed at 100 days age, the uterine growth response of 2.0 microgram estrone was inhibited by desoxycorticosterone acetate but unaffected by cortisone acetate (3). It is clear from above mentioned reports that as yet no general agreement has been reached regarding the nature of influence of adrenocortical hormones on female sex organs.

In the present series four corticosteroids *viz.* prednisolone, triamcinolone, dexamethasone and hydrocortisone have been studied to determine the exact effect of adrenal cortical hormones on gonads of female rats and to evaluate the relative potency of different semi-synthetic corticoids on the basis of comparative study on gonads.

## MATERIALS AND METHODS

Albino female rats weighing 80 to 100 gm. from Central Drug Research Institute colony were used in this experiment. All rats were maintained under uniform laboratory condition throughout the experimental period. A total number of thirty rats were divided in five groups containing six rats in each group. A detailed plan of treatment of animals is given below :—

Group I. Normal control in which no drug was given.

Group II. Treated with prednisolone (0.1 mg./rat/day for 15 days).

Group III. Treated with triamcinalone (0.1 mg./rat/day for 15 days).

Group IV. Treated with dexamethasone (0.1 mg./rat/day for 15 days).

Group V. Treated with hydrocortisone (0.1 mg./rat/day for 15 days).

All cortical hormones were injected by subcutaneous route. On the 16th day of treatment *i.e.* 24 hours after last injection, animals were sacrificed and following observations were made.

A. Weight of the following organs were taken :—

(1) Uterus—to eliminate the effect of natural variation in the size of uterus a definite length of uterus was used. In each case, left horn of uterus was taken and exactly 2 cm. was dissected out from cervix.

(2) Ovary.

B. Following biochemical investigation was performed :—

Alkaline phosphatase activity of ovarian tissue was done by the method of Fiske and Subba Row (4).

C. Histological study of ovary was undertaken. For histological study tissues were fixed in Bouin's fluid and serial paraffin sections were stained with hemotoxylin and eosin.

#### RESULTS

The maximum reduction of uterine weight was seen in triamcinalone treated group. (Table I)

TABLE I

*Changes in uterine and ovarian weight (mg/100 gm of body weight) of adult female albino rats after treatment with different adrenal cortical hormones*

	Normal Control	Predni- solone	Triam- cinalone	Dexa-; methasone	Hydro- cortisone
Uterine weight	22.2	12.3	6.8	17.7	8.6
Mean $\pm$ S.E.	$\pm$ 1.32	$\pm$ 0.7	$\pm$ 0.33	$\pm$ 0.88	$\pm$ 0.55
Ovarian weight	13.5	12.3	8.3	12.61	7.3
Mean $\pm$ S.E.	$\pm$ 0.53	$\pm$ 0.39	$\pm$ 0.44	$\pm$ 0.49	$\pm$ 0.34

The difference of uterine weight between this group and normal control was highly significant ( $P < 0.01$ ). Hydrocortisone treatment also caused marked depression of uterine weight ( $P < 0.01$ ), although it was less potent than triamcinolone. Prednisolone treatment also produced statistically significant reduction of uterine weight. However dexamethasone exerted minimum influence. The ovarian weight of hydrocortisone treated rats were most adversely affected (Table I). The reduction of ovarian weight caused by hydrocortisone was highly significant ( $P < 0.01$ ). Triamcinolone treatment also produced statistically significant inhibition of ovarian weight. The effect of dexamethasone and prednisolone on ovarian weight were not statistically significant. Regarding ovarian Alkaline Phosphatase in hydrocortisone and triamcinolone treated groups a significant depression of enzyme activity was noticed ( $P < 0.01$  in both cases) (Table II). Prednisolone and dexamethasone did not cause any significant alteration of enzyme activity.

TABLE II

Changes in alkaline phosphatase concentration of ovary (mg. /gm./1hr) of adult female albino rat after treatment with different adrenal cortical hormones

	Normal Control	Prednisolone	Triamcinolone	Dexamethasone	Hydrocortisone
Alkaline Phosphatase of ovary;	4.1	3.4	2.5	3.8	2.2
Mean $\pm$ S.E.	$\pm$ 0.04	$\pm$ 0.02	$\pm$ 0.02	$\pm$ 0.04	$\pm$ 0.02

Histology of ovary :—No histological change was noticed in any group treated with corticosteroids.

#### DISCUSSION

The present study indicates an inhibitory influence of corticoids on sex organs of female rats. Although histological study of ovary did not show any change, ponderal and biochemical alteration caused by all corticoids, particularly by hydrocortisone, is highly significant. It is interesting to note that Lohmeyer and Vasterling (5) could not detect any histological change in the ovary of prednisolone treated rats although they reported complete absence of fertility in them. Such inhibitory influences of corticoids on gonads is essentially in agreement with the work of similar nature undertaken by Donnet *et al.* (2)

Alteration of Alkaline phosphatase activity clearly indicates inhibitory influence of corticoids on the ovarian activity and most spectacular inhibition of enzyme activity is noted in hydrocortisone treated group and least in dexamethasone treated group. Thus, both biochemical and morphological changes are in agreement with each other.

It is to be decided whether these corticoids exert any direct action on ovary and inhibit the formation or release of oestrogen at graffian follicle and changes in the uterine weight is due to low level of oestrogen.

But it is also possible that the high concentration of corticosterone may inhibit, either secretion or release of gonadotrophic hormone, which might be responsible for adversely affecting the ovary.

In the triamcinolone and hydrocortisone treated group reduction in the uterine weight runs parallel to reduction in the ovarian weight and inhibition of alkaline phosphatase activity. It is therefore possible, that effects of triamcinolone and hydrocortisone on uterus are mediated through ovary. But in prednisolone and dexamethasone treated group reduction of uterine weight is not accompanied by reduction of ovarian weight or inhibition of alkaline phosphatase activity of the ovary. Therefore, effect of these hormones on uterus can not be explained by any mechanism involving the ovary. It is possible, that prednisolone and dexamethasone act by antagonising the effect of oestrogen at the level of target tissue and if such antagonism exists, inhibition of uterine weight without any change in ovarian weight or enzyme activity can be explained.

It is also interesting to note that although hydrocortisone is least potent glucocorticoid used in the present series, it is capable of producing most adverse effect; and least harmful effect is produced by dexamethasone which is most potent glucocorticoid used in this experiment.

#### SUMMARY

Effect of four corticosteroids, namely prednisolone, triamcinolone, dexamethasone, and hydrocortisone were studied in adult female albino rats. Parameters of study were uterine and ovarian weight, alkaline phosphatase activity of ovary and histology of ovary. In both biochemical and morphological studies an inhibitory effect of all corticosteroids were noted although no detectable change in the histology of ovary was noticed. Out of four corticosteroids used in this study hydrocortisone produced most prominent inhibitory effect and least adverse effect was produced by dexamethasone.

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#### REFERENCES

1. Blumenthal, H.T., J.P. Vaeth and S.D. Soule. Effect of non-ovarian hormones on the endometrium of castrate guineapigs. *J. Gerontol.* **13**:261, 1958.

2. Donnet, V., J.M. Chevalier, J.C. Duflo and M. Jacquin. Action de la cortisone sur l'appareil genital femelle. II. Animaux a ovulation provoquee (Lapine). *Compt. rend. soc. biol.* **154**:1028, 1960.
3. Edgren, R.A. and D.W. Calhoun. Estrogen antagonisms. The effects of various steroids on estrone-induced uterine growth in spayed rats. *Endocrinology.* **68**:633, 1961.
4. Fiske, C.H. and Y. Subba Row. The colorimetric determination of phosphorus. *J Biol. Chem.* **66**:375, 1925.
5. Lohmeyer, H. and H.W. Vasterling. Cortisone and fertility. *Z. Geburtshilfe (u. Gynokil), Beilageheft Beitrage zur Fertilitat und Sterilitat.* **87**:1960.
6. Pallot, G. and K. Domanowsky. Action experimental des corticoides non androgenes DCA et cortisone sur les glandes oestrogenes et progestatives et sur l'histologie dynamique de l'ovaire adulte. *Compt. rend soc. biol.* **147**:1434, 1953.