

Response of Hypophysectomized Immature Male Rats to Pregnant Mare Serum.*†

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Hypophysectomized mature and immature male rats will respond to pregnant mare serum as shown by the maintenance or restoration of spermatogenic function and the enlargement of the accessory reproductive organs.¹⁻⁵ In previous studies on hypophysectomized rats, the adult was generally used and treatment extended for a long period of time. The investigation here reported was undertaken to study the effects of pregnant mare serum on hypophysectomized immature male rats that were all subjected to a short (5-day) injection period. This study was of interest in view of results previously obtained in hypophysectomized immature female rats in which it was shown that dosage variation alone would produce markedly different types of ovarian stimulation.^{6,7} Furthermore, Fevold⁸ uses the male rat as an assay method for luteinizing hormone as determined by seminal vesicle weight increase.

Immature male rats ranging from 30 to 36 days of age were hypophysectomized. Body weights ranged from 71 to 86 g at the

time of operation whereas the body weight at the time of autopsy (10 days later) ranged from 65 to 83 g. An interval of 5 days was allowed to elapse after hypophysectomy in all cases. The hormone was injected subcutaneously once daily for 5 days and the animals autopsied 24 hours after the last injection. All pituitary capsules were serially sectioned, stained with Mallory's connective tissue stain and examined microscopically. Only data from completely hypophysectomized animals are presented. Weights of the adrenals, testes and seminal vesicles (including the coagulating gland and any contained fluid) were taken.

Pregnant mare serum (Gonadin)[‡] was administered in 6 different total doses to groups of 7 to 13 animals each. Testis weight increased in most animals receiving hormone when a comparison is made with untreated hypophysectomized rats, 10 days postoperatively. However, when a comparison is made with the testis weight of animals 5 days postoperatively, at which time injections were started, it is obvious that the effect of the hormone is essentially that of maintenance (Table I). Spermatids and spermatozoa were absent.

The lowest dose of hormone tested caused a 100% increase in seminal vesicle weight. Administration of larger doses resulted in a more pronounced response. However, it should be pointed out that the 25 and 50 r. u. total dosages were equally effective in their action on seminal vesicle weight (Table I).

It has been shown that PMS when administered to hypophysectomized immature female rats in a manner identical with the methods used here in males will produce a varied ovarian effect depending upon the

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³ Greep, R. O., *Cold Spring Harbor Symposium*, 1937, **5**, 136.

⁴ Liu, S. H., and Noble, R. L., *J. Endocrinology*, 1939, **1**, 7.

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⁶ Leatham, J. H., *Proc. Soc. Exp. Biol. and Med.*, 1940, **43**, 590.

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⁸ Fevold, H. L., *Cold Spring Harbor Symposium*, 1937, **5**, 93.

[‡] Pregnant mare serum, Gonadin, was generously supplied by Dr. D. H. Wonder, Cutter Laboratories, Berkeley, California.

TABLE I.

Influence of Pregnant Mare Serum on Hypophysectomized Immature Male Rats.

Total dose	No. of rats	Avg organ wt (mg $\pm$ E _m)	
		Testes	Sem. ves.
0	7	231	7.6 $\pm$ 0.6
2.5	10	443	14.9 $\pm$ 2.1
5.0	13	335	17.9 $\pm$ 2.9
12.5	7	273	19.3 $\pm$ 3.0
25.0	9	409	30.7 $\pm$ 2.8
50.0	11	366	29.9 $\pm$ 4.0
100.0	10	451	41.8 $\pm$ 4.5
Control rats 5 days after hypophysectomy		365	7.5
Unoperated control rats 35 days of age		718	13.2

E_m = mean deviation of the mean.

dosage injected.⁶ A low dose (10 r. u.) causes marked thecal luteinization with little growth of follicles. A larger dose (25 r. u.) results in the development of large vesicle

follicles and slight thecal luteinization whereas further dosage increases (50 r. u.) causes the formation of corpora lutea. The lot of hormone used in these experiments produced the same effect in the hypophysectomized female rats as those just described. It was of interest to find that a 25 r. u. dosage which produces a 10-fold ovarian weight increase and primarily a follicle stimulating effect also causes a 4-fold increase in seminal vesicle weight in hypophysectomized male rats. These results indicate that the potency of a dosage of pregnant mare serum as determined by its action on the ovary does not indicate its ability to increase seminal vesicle weight.

Summary. Pregnant mare serum maintains testis weight and stimulates seminal vesicle weight in hypophysectomized male rats treated for a 5-day period. These data are compared with those from similarly treated female rats.

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Reproducible Diuresis and Chloruresis for Bioassay of Antidiuretic Activity.

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For the bioassay of antidiuretic activity it is essential that control observations shall provide a diuresis which is both reproducible and quantitative. In a previous communication¹ certain results obtained by a satisfactory method were given. It is the purpose of this paper to describe in greater detail a comparison of the various procedures explored. In agreement with the prediction of Silvette² it appears that extracts of the posterior lobe of the pituitary gland can be assayed more accurately by measuring

urinary chloride excretion than by measuring the inhibition of water excretion.

The rat method of assaying the antidiuretic activity of extracts of the posterior lobe of the pituitary gland was introduced by Burn.³ Subsequently many modifications have been described both in the manner of producing hydration and in the calculation of results. These procedures have been employed to assay the antidiuretic activity of urine, blood serum and pituitary extracts.

Three different methods of hydration were chosen for comparison. (A) Gilman and Goodman⁴ administered a preliminary "hy-

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³ Burn, J. H., *Quart. J. Pharm. and Pharmacol.*, 1931, **4**, 517.

⁴ Gilman, A., and Goodman, L., *J. Physiol.*, 1937, **90**, 113.