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Inhibitory Effects by the Hypophysis of Rats Following Injections of Pregnant Mare Serum Hormone.*

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Regarding the reciprocal pituitary-gonad relationship, most investigators agree that prolonged treatment with estrogenic substances inhibits the secretion of gonadotropic hormones from the hypophysis. Møller-Christensen¹ and du Shane *et al.*,² working with rat parabiosis, have found that the hypophysis exerts an inhibitory effect on overstimulated ovaries. The experiments here reported are harmonious with these findings in parabiotic rats.

1. *Controls.* Both normal and spayed (2-17 weeks) adult female rats were bled and the serum separated by coagulation. The gonadotropic action of the serum was tested by injecting 1 cc. of rat serum, in 5 divided doses, into immature female mice. The ovaries of the mice were weighed 96 hours after the first injection. As may be seen from the table, the normal rat sera (29 rats in 31 mice) contained no detectable gonad-stimulating hormones and the castrate rat sera (29 rats in 27 mice) but small amounts.

2. *Treated rats.* Similar rats, normal and spayed (2-17 weeks), were then injected with 50 mouse units daily of a gonadotropic hormone from pregnant mares' serum ("Antex" Leo‡). Following 9 to 86 days' treatment, the rats were sacrificed 24 hours after the last injection and the serum tested on mice. The treated normal rat sera (50 rats, 49 mice) gave slightly positive responses whereas the treated spayed rat sera (32 rats, 33 mice) contained about 5 times as much of the gonad-stimulating factor (Table). There was no apparent relationship between the length of treatment of

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¹ Møller-Christensen, E., *Acta Path. et micr. Scand.*, 1935, Suppl., 22.

² du Shane, G. P., *et al.*, *Proc. Soc. Exp. Biol. and Med.*, 1935, **33**, 339.

‡ "Antex" (manufactured by the "Løvens kemiske Fabrik," Copenhagen) is a purified gonadotropic hormone preparation from the serum of pregnant mares. One mouse unit is the minimum amount of hormone which will double the weight of the ovaries in 3-weeks-old-mice.

TABLE I.
Gonadotropic Effect in Infantile Female Mice of 1 cc. of Serum from Donor Rats
After Different Treatment.

Type of rat	Hormone treatment*	No. of rats	Aver. B.W. gm. at autopsy	No. of mice injected	Wt. of 1 mouse ovary in mg.		
					Aver.	Min.	Max.
Normal	None	29	146	31	1.1	—	—
"	Antex	50	146	49	1.8	1.1	2.7
Spayed	None	29	140	27	1.5	1.2	1.8
"	Antex	32	152	33	5.8	3.7	6.9
"	Antex + estrin	10	159	10	2.8	1.9	3.9
Hypsect.	Antex	9	127	10	5.4	2.7	8.3
" + spayed	"	12	127	14	6.5	4.4	9.6
" " " " + estrin	"	9	123	9	5.9	4.0	9.2

*Dosage described in text.

the donor rat (9 to 86 days) and the gonadotropic effect of its serum.

To eliminate the possibility that the gonadotropic factor already present in the spayed rats might augment the injected material, and thus account for the greater effects obtained in the injected spayed rats, equal amounts of "Antex" were mixed with serum from untreated normal and spayed rats and tested on mice (142 mice). Spayed rat serum with "Antex" gave about 50% larger mice ovaries than normal rat serum with "Antex." Similarly, simultaneous injections of untreated spayed rats' serum and serum of normal "Antex"-injected rats gave also about 50% larger mice ovaries than the serum of normal "Antex"-injected rats alone (21 mice). Both of these augmentation reactions were much less, however, than the responses obtained from the serum of spayed rats treated with mare serum hormone.

3. *Hypophysectomized-treated rats.* By the use of hypophysectomized rats§ it is thought possible to eliminate altogether the presence of any but injected gonad-stimulating substance. Nine non-spayed and 12 spayed, hypophysectomized animals were treated in the same way as the non-hypophysectomized had been. The gonadotropic hormone content of the sera of the spayed and non-spayed groups was nearly identical. (The ovaries of the treated hypophysectomized rats were different in no significant manner from those of the treated normals.)

The figure summarizes this material. All 4 types of rats are

§ In 8 of the 30 hypophysectomized rats the microscopical examination of the capsules revealed small fragments of pituitary tissue, but as the serum of these rats did not differ in any respect from that of the complete ones they are not excluded from the experiments.

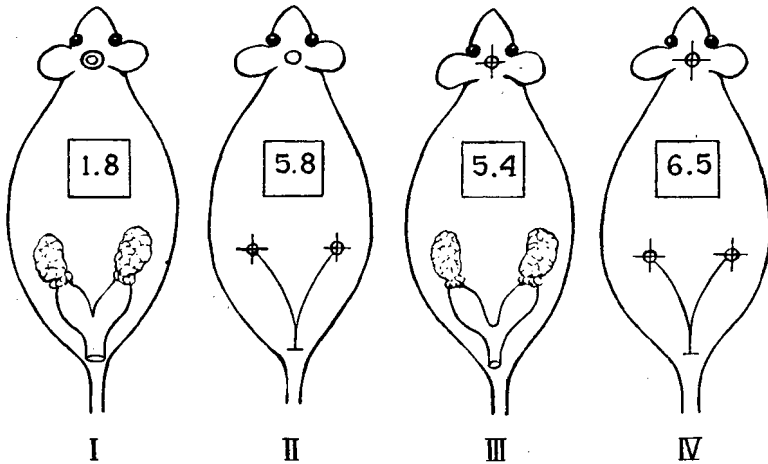


FIG. 1.

The gonadotropic potency of the serum of rats treated with gonadotropic hormone from pregnant mares.

- I. Normal.
- II. Spayed.
- III. Hypophysectomized.
- IV. " " -spayed.

"Antex"-treated. The amount of gonadotropic hormone in the serum is indicated by the number within the square (the *average* weight of *one* ovary from the test mice). The serum titre is high in the spayed rats, in the hypophysectomized and in the hypophysectomized-spayed rats, indicating that the difference between the normal injected and the spayed injected rats cannot be due to a hyperfunction of the castrate hypophysis or to a utilization of the injected hormones by the ovaries. Only in the presence of both organs (ovaries and hypophysis) is there a reduced amount of gonadotropic substance in the serum of rats treated with pregnant mare serum.

In normal, mare-serum treated rats the ovaries were markedly stimulated and the pituitary gland was greatly enlarged, as previously reported by Evans *et al.*³ On the other hand, there was no hypophysis weight increase in the spayed rats treated with "Antex." This suggested some action on the hypophysis by the stimulated ovaries and also suggested that such action and the resulting enlarged hypophysis might be correlated with the decreased serum titres, found only in the normal, treated animals.

4. *Estrin treated.* To test these suggestions, 10 spayed rats were treated with estrin ("Progynon B," 500 I.U. daily, 14 days) as well as with "Antex." Hypophysis enlargement was found, as

³ Evans, H. M. *et al.*, *Univ. Calif. Publications in Anat.*, 1934, **1**, 161.

in normal treated rats. Similarly, the serum of these animals also contained low titres of gonad-stimulating material, comparable to treated normal rats, with estrin producing ovaries. Nine hypophysectomized spayed animals, identically treated, gave high serum titres in spite of estrin injections (Table).

5. *Conclusion.* It appears that the hypophysis under the influence of estrin, whether supplied by injections or by overstimulated ovaries, actually inhibits possibly through the intermediary of some other endocrine gland the action of gonadotropic hormone.

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Transmission of Nutritional Muscular Dystrophy to Rabbits
in Utero.

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When young rabbits are placed upon muscle-dystrophy producing Diet 11, the majority die within a period of several months.¹ Rarely the disease runs a protracted course; the animals may survive for a year, only to succumb eventually with characteristic degeneration of the skeletal muscles. One such adult dystrophic rabbit successfully completed gestation and gave birth to living young. This exceptional event, has permitted us to observe that nutritional muscular dystrophy may be passed on from mother to offspring.

Rabbit 241 was born in the laboratory on Jan. 15, 1935. On Feb. 19th, it was weaned and given Diet 11.* A biopsy from the thigh muscles was taken on Jan. 6th, 1936, when the animal had attained a weight of 2.4 kilos. A few necrotic fibers were found in each low power field. The muscle creatin was 540 mg.—within the normal range. Two subsequent biopsies on Nov. 19th and Dec. 11th showed little progression of the lesions.

¹ Goettsch, M., and Pappenheimer, A. M., *J. Exp. Med.*, 1931, **54**, 167.

* Diet 11. Rolled oats (Quaker).....355 parts
Wheat bran (Pillsbury).....180 "
Casein (Merek technical).....75 "
Lard80 "
Cod liver oil (Mead-Johnson).....10 "
NaCl10 "
CaCO₃15 "