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Quantitative Difference in a Rabbit-Ovulating Dose of Prolan and Anterior Pituitary Extract.

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It was previously reported¹ possible to obtain follicular development and corpora lutea formation in immature female rats with a dose of pregnancy urine which was inadequate to induce ovulation in an adult female rabbit in heat. Friedman² has recently shown that the ovulating dose of Prolan (from pregnancy urine) is equal to approximately one rat unit per kilogram of body weight of the rabbit. This report will attempt to show that this quantitative relationship does not hold when using an anterior pituitary extract.

The extract used in these experiments was the water soluble fraction of a pyridine extract of sheep anterior pituitary, capable of producing follicles and a few corpora lutea in immature rat ovaries.³ It was administered in 1 cc. of distilled water intravenously into adult rabbits in heat and 15-20 hours later the ovaries were examined grossly for ovulation. The immature rats were injected subcutaneously (0.25 gm. doses) twice daily for 5 days and killed on the beginning of the 6th day. Sixteen rabbits and 9 rats were used in these experiments.

In the first group, doses of the extract from .025 gm. equivalent of dry powdered gland to .0025 gm. gave positive ovulation. Two

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¹ Leonard, S. L., *Am. J. Physiol.*, 1931, **98**, 406.

² Friedman, M., *J. Exp. Pharm. and Therap.*, 1932, in press.

³ Evold, H. L., Hisaw, F. L., and Leonard, S. L., *Am. J. Physiol.*, 1931, **97**, 291.

months later the M.O.D. (minimal ovulating dose) was found to be .005 gm., indicating a slight deterioration of the extract. However, if amounts of the same extract equal to .025 or .0125 gm. of anterior lobe were given to sexually immature female rats, no apparent morphological or physiological changes were produced in the ovaries after 5 days' treatment (Table I). These amounts are

TABLE I.
Failure of a Rabbit Ovulating Dose of Anterior Pituitary Extract to Stimulate Ovaries of 22-day-old Rats.

Rat	Total Dose S.A.P. 1	No. Days Injected	Vagina at Autopsy	Wt. of Uterus and Vagina	Wt. of Ovaries
				gm.	gm.
GH5971 a	Control	—	Closed	.0535	.0120
b	.025 gm.	5	"	.0625	.0105
c	.025 gm.	5	"	.0835	.0123
d	.0125 gm.	5	"	.0610	.0095
e	.0125 gm.	5	"	.0770	.0110

several times the M.O.D. for rabbits, which emphasizes the difference from Prolan. The experiment was repeated using a different batch of hormone prepared in the same manner and the results were comparatively identical, although the M.O.D. in this case was between .005 gm. and .0075 gm. Again, several times the M.O.D. of the extract was without effect on the immature rats.

It should be pointed out that the rabbits must be isolated for 15-20 days or more before they are used again. In another series of 4 rabbits, it was found that the M.O.D. was not sufficient to induce ovulation in an adult rabbit which had been stimulated 10 days previously, even though grossly the ovaries contained apparently normal ripe follicles. A larger dose, however, will induce ovulation under such conditions. Therefore, a standard rabbit should be adopted in determining the M.O.D. of these extracts.

Conclusions. 1. The ovulating dose of an anterior pituitary extract for rabbits is very much less than that of Prolan when the potency of these 2 substances is standardized on immature female rats. 2. This difference in quantitative activity of Prolan and anterior lobe extract suggests a physiological difference between the 2 substances.