Prolactin-Induced Morphological Luteal Regression Unaffected by LH*† (34006)

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Luteinizing hormone was reported to decrease the size of nonfunctional corpora lutea (1, 2). This activity was lost with further purification (3). LH has been shown to terminate progesterone secretion from corpora lutea of hypophysectomized pituitary-grafted rats (4) and to decrease the size of the corpora lutea. Malven and Sawyer (4) reported that NIH prolactin was capable of reducing the size of nonfunctioning corpora lutea in hypophysectomized rats. Thus, the original observations that corpora lutea decreased in size may have been dependent upon the amount of prolactin contained in these preparations of LH. Luteinizing hormone may well terminate progesterone secretion. The observed luteal regression associated with cessation of progesterone secretion may not be a function of LH but rather, the effect of continuing prolactin secretion from the graft. In an attempt to determine whether LH influences the rate of prolactin-induced luteal regression, the following experiment was conducted.

Materials and Methods. The rats used were obtained at 55 days of age from the Holtzman Company and were housed in a light-, temperature-, and humidity-controlled room. Feed and water were available *ad libitum*. Vaginal smears were observed daily for approximately 2 weeks. There were seven experimental groups composed of 6 to 7 animals each. Animals of group A were not hypophysectomized and were sacrificed on the day of metestrus as a primary control. Animals of group B through G were hypophysectomized on the day of metestrus. Group B animals were sacrificed 2 days after hypophysectomy, the day groups C through G received the first of two daily subcutaneous injections of 0.2 ml of the saline vehicle alone, 2.5 IU of prolactin (NIH-P-S-7) or this amount of prolactin plus 0.5, 2.5, or 7.5 μg NIH-LH-S-8 in 0.2 ml saline. The rats were sacrificed the day after the last treatment. The ovaries were weighed and fixed in Bouin's fluid for histological study. Tissues were sectioned and stained with hematoxylin and eosin. Ovarian weights were analyzed statistically by analysis of variance and the Duncan-Bonner multiple range test (6).

TABLE I. Ovarian Weights of Animals Hypophysectomized during Metestrus and Treated with Prolactin Alone or with Prolactin and LH.

Group	Day of sacrifice after hypophysectomy	No. rats	Treatment[a]	Ovarian wt (mg) ± SE
A	0	7	None	54.5 ± 3.2
B	2	7	None	51.9 ± 1.6
C	8	7	0.2 ml saline, b.i.d.	38.1 ± 1.4
D	8	7	2.5 IU prolactin, b.i.d.	27.6 ± 2.3
E	8	7	2.5 IU prolactin and 0.5 μg LH, b.i.d.	28.7 ± 2.3
F	8	7	2.5 IU prolactin and 2.5 μg LH, b.i.d.	27.1 ± 2.8
G	8	7	2.5 IU prolactin and 7.5 μg LH, b.i.d.	28.0 ± 2.0

[a] All injections given in 0.2 ml saline twice a day, days 2, 3, 4, 5, 6, and 7, subcutaneously; prolactin, NIH-P-S-7 and LH, NIH-LH-S-8 carried in 0.2 ml saline.

Results and Discussion. Hypophysectomy causes the ovary to decrease in weight with

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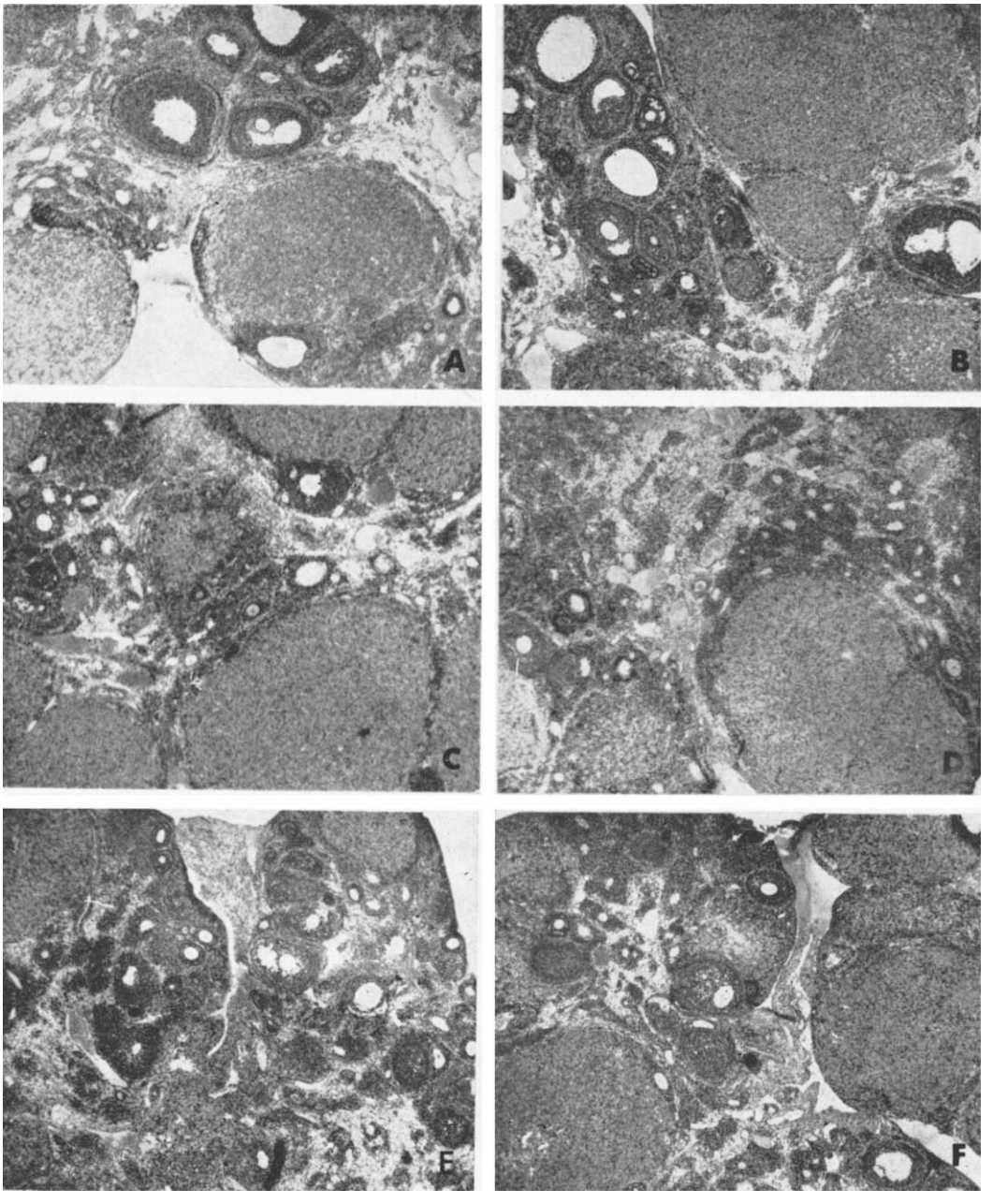

FIG. 1. Histological sections of ovaries of rats (×73). The rats were killed on the day of metestrus or hypophysectomized that day and killed subsequent to further treatment. A. Control killed on the day of metestrus, ovaries contain corpora lutea and vesicular follicles. B. Control, killed 2 days after hypophysectomy. Corpora lutea appear to compose a greater percentage of the ovary due to the reduced follicular size. C. Control, killed 8 days after hypophysectomy but received 0.2 ml saline twice daily last 6 days. Follicles are further reduced in size and corpora lutea compose greater proportion of whole ovary. D. Treated as C except prolactin (2.5 IU/0.2 ml b.i.d.) was injected in saline for the 6 days. E and F. Treated as C except LH, 2.5 and 7.5 μg respectively was given with the injected prolactin. Prolactin reduced luteal size and LH treatment had no effect.

time (Table I). The weight loss was significant ($p<.05$) 2 days after operation and became highly significant at 8 days ($p<.01$). The loss between days 2 and 8 was significantly different ($p<.01$). Prolactin alone reduced ovarian weight compared to hypophysectomized controls ($p<.01$). All animals that received prolactin with or without LH were not significantly different. These results illustrate that prolactin accelerated loss of ovarian weight after hypophysectomy and that LH was without influence. It was noted at autospy, and was further defined by the histological sections, that the corpora lutea of the ovary were smaller in prolactin-treated animals. Comparison of photomicrographs of representative sections (Fig. 1, C vs. D, E, and F) illustrate the diminished size of the corpora lutea due to prolactin treatment. Since follicular regression was equivalent in all ovaries of rats in groups C through F, it is assumed that the weight change observed in rats given prolactin was due to regression of the luteal tissue present at the time of hypophysectomy. The regression of follicular size due to hypophysectomy is illustrated by photomicrographs A, B, and C. It is concluded that although LH is able to terminate prolactin-maintained progesterone secretion in the rat it does not influence the rate at which prolactin induces morphological regression of nonfunctional corpora lutea.

Summary. The ovary of the mature rat undergoes some weight loss during the first 8 days after hypophysectomy due to follicle degeneration. Administration of 2.5 IU of NIH-P-S-7 prolactin twice daily from the second day after hypophysectomy causes a more rapid reduction in ovarian weight due to the regression of luteal bodies. The administration of 0.5, 2.5, or 7.5 μg NIH-LH-S-8 luteinizing hormone with prolactin did not influence this luteolysis.

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