

Luteal Regression with Rat Prolactin¹ (37463)

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Rat prolactin (1.5 IU b. i. d.) will maintain luteal function in hypophysectomized rats for a longer span of time than the same dose of ovine prolactin (1) due to the fact that the ovine prolactin is antigenic (2). Ovine prolactin is also luteolytic; as little as 2.5 IU b. i. d. administered twice daily to hypophysectomized rats will reduce the size of the corpora lutea (3). The response is dose related (4). The present study was undertaken to determine whether rat prolactin in addition to being luteotrophic is also luteolytic as is heterologous ovine prolactin.

Method. Mature cyclic Sprague-Dawley rats (Charles River) were kept in a temperature, humidity and light (14 L, 10 D)-controlled room where food and water were supplied *ad libitum*. Estrous cycles were determined by vaginal smears obtained daily for at least 1 wk prior to hypophysectomy. On the day of metestrus (Day 1) some animals were sacrificed to serve as controls (Group 1); others were hypophysectomized and assigned to one of three additional groups. Hypophysectomies were performed under ether anesthesia by the parapharyngeal approach. All rats remained untreated on Days 1 and 2 after hypophysectomy. On Day 3, some hypophysectomized rats were sacrificed as operation controls (Group 2). The remaining animals were injected subcutaneously with 0.2 ml saline (Group 3) or 2 IU rat prolactin in 0.2 ml saline (Group 4) twice daily on Days 3 through 9 and sacrificed on the morning after the last injection. At autopsy, the ovaries of each animal were cleaned of extraneous tissue and weighed. Whole ovaries were fixed in Bouin's fluid, imbedded in paraffin, sectioned at 7 μ m

and stained in hematoxylin and eosin for microscopic evaluation. The sella turcica of each animal was searched for pituitary remnants with a binocular loupe. Only completely hypophysectomized rats were included in the data. Ovarian weights were compared by analysis of variance.

Results. Hypophysectomy reduced the ovarian weights in 2 days (Table I). The weight of ovaries of hypophysectomized rats which received saline for 7 days were not significantly smaller than ovaries from animals hypophysectomized for 2 days. However, the ovaries of rats treated with rat prolactin weighed significantly less than those of saline-injected controls. That the corpora lutea in the ovaries of the prolactin-treated rats were also reduced in size was evident macroscopically. This was further substantiated when histological sections of the treated and control ovaries were viewed under low magnification (Figs. 1, 3). The corpora lutea (CL') were smaller and comprised less of the total ovary in rats treated with prolactin than in rats treated with saline. Higher magnification revealed fewer lutein cells (L') with a higher incidence of pyknotic nuclei (Figs. 2, 4) and many prominent fibroblasts (F'). The cytoplasm of the luteal cells of saline-treated rats was of uniform consistency while that of luteal cells in prolactin-treated animals was vacuolated and appeared more coarse and granular.

Discussion. It has been shown previously (3-6) that heterologous prolactin induces morphological luteal regression in the rat. The current report demonstrates that exogenously administered rat prolactin also induces luteolysis in the rat. That rat prolactin has this capacity was initially suggested by Sloan and Malven (4) who observed struc-

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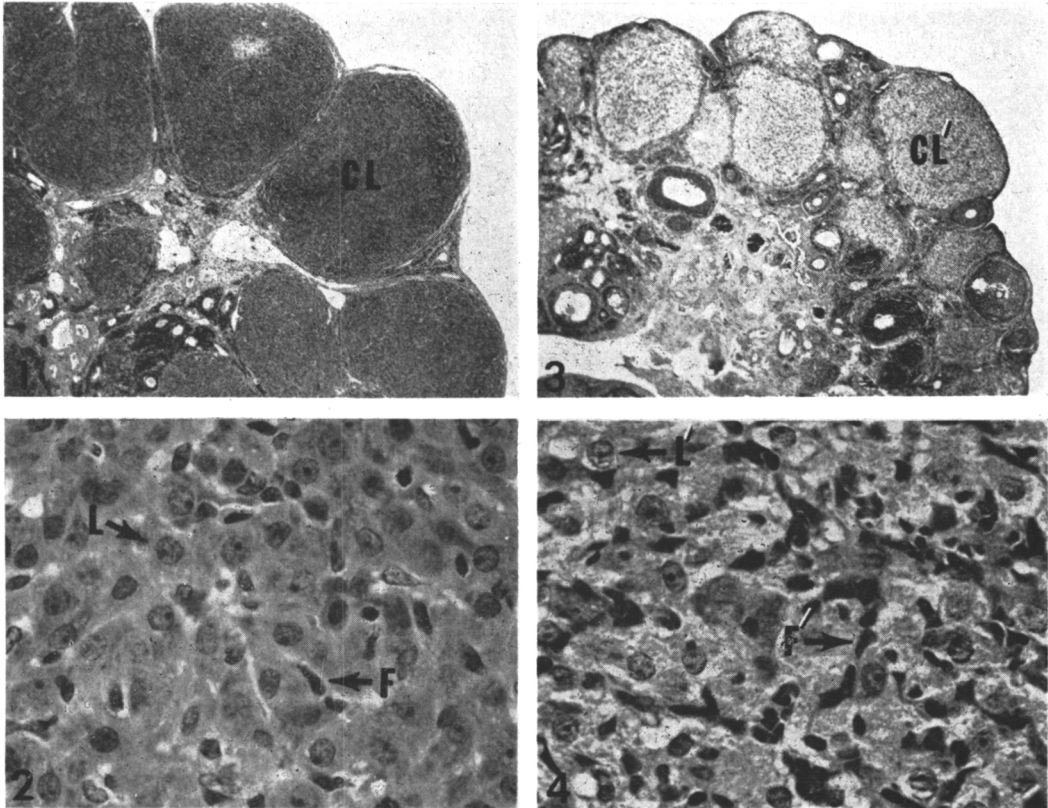


FIG. 1. Micrograph ($\times 25$) of ovary from a rat treated with saline (0.2 ml b. i. d., Days 3-9) showing corpora lutea (CL). Figs. 1-4. Histological sections from ovaries of hypophysectomized rats sacrificed on Day 10.

FIG. 2. Higher magnification ($\times 470$) of a corpus luteum in Fig. 1 showing luteal cells (L) and few fibroblasts (F).

FIG. 3. Micrograph ($\times 25$) of ovarian tissue from a rat treated with prolactin (2 IU b. i. d., Days 3-9) showing reduced corpus luteum size (CL').

FIG. 4. Higher magnification ($\times 470$) of a corpus luteum in Fig. 3 showing luteal cells (L') and increased numbers of fibroblasts (F') denoting a reduction of the luteal cell population.

tural luteolysis in hypophysectomized rats following the grafting of a pituitary beneath the kidney capsule. Such grafts are known to secrete prolactin. LH contained in the graft at the time of transfer could not have contributed to the results (8, 9). The luteolysis induced by treatment with rat prolactin was evidenced by a diminution in size of the corpora lutea, loss of ovarian weight and proliferation of fibroblasts as seen in histological sections. The fibroblast population appeared to increase at the expense of luteal cells.

Each estrous cycle of the rat results in a new crop of corpora lutea formed under the

influence of LH. These newly formed corpora lutea secrete progesterone for a limited time through early diestrus (10-12). Progesterone secretion is dependent upon the continuing presence of prolactin (13-15). During the succeeding estrous cycles these new corpora lutea undergo luteal regression. The regression is always most marked during the first succeeding cycle and continues over the subsequent 3 or 4 cycles stepwise (16). It has been suggested that although LH can initially increase ovarian progestin secretion the latent effect is to reduce this secretory activity (2, 12, 17). Thus corpora lutea with diminished functional capacity become susceptible to the

TABLE I. Effect of Rat Prolactin on Ovarian Weight in Hypophysectomized Rats.^a

Group	Treatment	No. of rats	Ovarian wt (mg; mean \pm SE)
1	None	7	74.5 \pm 5.3
2	APX for 2 days	7	50.3 \pm 3.6 ^b
3	APX 2 days + 7 days saline	7	42.4 \pm 2.6 ^b
4	APX 2 days + 7 days prolactin	7	24.3 \pm 1.4 ^{b,c}

^a Saline, 0.2 ml twice daily Days 3 through 9. Prolactin, 2 IU in 0.2 ml saline given twice daily Days 3 through 9.

^b Significantly different ($p < 0.001$) from Group 1.

^c Significantly different ($p < 0.01$) from Groups 2 and 3.

luteolytic action of the cyclicly elevated output of prolactin (18). This then becomes the mechanism in the rat for disposing of older corpora lutea.

Summary. Rats were hypophysectomized on the morning of the day of metestrus and remained untreated for 2 days. One group was then sacrificed; another group received 0.2 ml saline twice daily for 7 days, and a final group received 2 IU rat prolactin twice daily for 7 days. These two latter groups were sacrificed the day after the last injection. Ovarian weights were significantly reduced ($p < 0.01$) by treatment with rat prolactin. Histological sections of the ovarian tissue revealed a reduction in corpus luteum size and in the number of luteal cells. These findings suggest that prolactin is involved in luteal regression in normally cycling rats.

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