Luteolytic Action of Prolactin During Estrous Cycle of the Mouse (36450)

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In the rat prolactin has been shown to exert a luteotropic action on newly formed corpora lutea and a luteolytic effect on older corpora lutea (1). During each estrous cycle of the rat, luteolysis of corpora lutea from previous cycles occurs (2, 3). Recent work from our laboratory has shown that the proestrous surge of prolactin during the estrous cycle is responsible for luteolysis of the old corpora lutea (4). Billeter and Flückiger (5) also reported a luteolytic action by prolactin when injected daily in cycling rats with an ergot drug (CB154) for 21 days.

In the mouse prolactin produces a luteotropic action on the corpora lutea (2), but a luteolytic action for prolactin has not been described. A brief report by Kwa and Verhofstad (6) states that during the estrous cycle of the mouse, blood prolactin rises beginning late in proestrus and reaches a peak early in estrus. It was of interest therefore to determine in the mouse whether inhibition of prolactin secretion by the drug ergocornine (EC) during proestrus and estrus could prevent luteolysis of the old corpora lutea, and whether concurrent administration of prolactin could induce luteolysis. EC previously was reported to decrease pituitary prolactin levels in the mouse (7) as well as in the rat (8, 9).

Materials and Methods. Mature 2–3-month-old virgin female Swiss-Webster mice (Spartan Research Animals, Haslett, MI) were housed in a temperature controlled (75 ± 1°F) and artificially illuminated (lights on from 5 a.m. to 7 p.m. daily) room, and given Wayne Lab Blox pellets and water *ad libitum*. Estrous cycles were followed by examining daily vaginal smears for 2 weeks prior to the beginning of the experiments, and only mice undergoing regular cycles were used. Ergocornine methanesulfonate (EC) base[2] was first dissolved in 70% ethanol and then in 0.9% saline to give a final volume of 4% ethanol. Ovine prolactin was dissolved in 0.9% saline.

Twenty mice were each injected ip with 200 μg EC daily, beginning on the last PM of diestrus prior to the expected day of proestrus and continuing for 3 days. On the afternoon of proestrus and on the morning of estrus 10 of the 20 mice were each injected subcutaneously with 1 mg prolactin.[3] A group of 10 control mice were each injected ip daily with the saline ethanol solution during the same period. At the end of treatment, on the first day of diestrus, the mice were killed and the ovaries were removed, cleaned, weighed, fixed in Bouin's solution and stained with hematoxylin and eosin. The number of corpora lutea were counted from a single mid-saggital section.

In another experiment, 16 mice were injected ip daily with 200 μg of EC/mouse beginning on the afternoon prior to the expected day of proestrus and continuing for three estrous cycles. During each cycle, 9 of the 16 mice were injected with 1 mg of prolactin on the afternoon of proestrus and on the morning of estrus during each cycle. A control group of 8 mice were injected daily for three cycles with the saline ethanol solution. The mice were killed on the first day of diestrus after the third cycle, and the ovaries were removed and prepared as in the first experiment.

Results. EC treatment during a single cycle (Table I) led to a significant increase in

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[2] Ergocornine methanesulfonate was kindly provided by Dr. M. Taeschler and Dr. E. Flückiger, Sandoz Ltd., Basel, Switzerland.

[3] NIH-P-S-8 ovine prolactin, 28 IU/mg.

TABLE I. Effects of Ergocornine (EC) and Prolactin During the Estrous Cycle on Corpora Lutea.

Treatment and no. of mice	Av Body wt (g)	Av Ovarian wt (mg)	Av No. of corpora lutea[a]
		One estrous cycle	
Controls (10)	22.4 ± 1.5	24.4 ± 3.2	6.0 ± 0.4
EC (10)	22.6 ± 1.6	23.2 ± 2.3	9.7 ± 0.7[b]
EC + prolactin (10)	22.7 ± 1.8	17.0 ± 1.5	5.3 ± 0.5[c]
		Three estrous cycles	
Controls (8)	36.9 ± 0.6	24.8 ± 1.0	6.9 ± 0.7
EC (9)	34.6 ± 0.5	23.9 ± 1.0	9.6 ± 0.8[b]
EC + prolactin (7)	34.3 ± 0.5	22.6 ± 1.0	6.2 ± 0.7[c]

[a] Represents single cross-section count.
[b] EC vs controls = $p < .05$.
[c] EC vs EC + prolactin = $p < .05$.

the number of corpora lutea (9.7 ± 0.7) compared to the number of corpora lutea (6.0 ± 0.4) in control mice. Injections of prolactin on the days of proestrus and estrus, in EC-treated mice resulted in a return of the number of corpora lutea to about the same number as in control mice. No differences were apparent in the appearance of the corpora lutea as a result of EC treatment. Ovarian weight was slightly reduced in the group given EC and prolactin compared to the other 2 groups. None of the groups differed significantly in body weight.

EC treatment during 3 cycles had the same effect as treatment during one cycle, resulting in a significant increase in number of corpora lutea compared to those in control mice. Prolactin administration to EC-treated mice on the day of proestrus and estrus during each of the 3 cycles resulted in a return of corpora lutea to about the same number as in normal mice. No significant differences were observed in ovarian or body weights in any of the 3 groups of mice.

Discussion. These results demonstrate that a reduction in prolactin secretion in cycling mice induced by EC results in an increase in number of corpora lutea, and that injections of prolactin on the days of proestrus and estrus returns the number of corpora lutea to normal. It is apparent therefore that prolactin promotes luteolysis of corpora lutea during the estrous cycle of the mouse just as it does in the rat (4, 5). Unlike the rat, the accumulation of corpora lutea in the ovaries in the mouse as a result of EC treatment was not accompanied by increased ovarian weight. We have observed that even injections of EC for 30 days into cycling mice did not result in increased weight of the ovaries and did not interrupt cycling, although the number of corpora lutea was increased (unpublished data). No obvious differences were observed in histological appearance of the corpora lutea of the mice treated with EC compared with the corpora lutea of control mice.

Although this study demonstrates a luteolytic role for prolactin during the estrous cycle of the mouse, it does not exclude possible involvement of other factors. Rothchild (10) provided evidence that LH may promote luteolysis of old corpora lutea in the rat under some conditions. Inasmuch as rats and mice continue to cycle normally during administration of EC, indicating continued secretion of LH and FSH, any role by either of these 2 gonadotropins on luteolysis of old corpora lutea would appear to be negligible. However, it is possible that LH may act synergistically with prolactin during the cycle to induce luteolysis of old corpora lutea.

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