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Prolonged Production of Ovarian Progesterone in Pseudopregnant Hamsters Bearing Deciduomata (38698)

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Deciduomata (DCRs) have been shown to prolong the hyperemic state of the corpora lutea (CL) of pseudopregnancy (PS) in hamsters (1). Hyperemia terminates on day 6 in the absence of DCRs (1) and progesterone levels decline at this time (2). Hyperemia ceases on day 7 in hamsters with DCRs (1) and the duration of PS as measured by the postponement of psychic estrus is not significantly affected by massive DCRs (3). However, the duration of PS in rats is significantly prolonged by DCRs (4) and the degree of prolongation is dependent on the amount of decidual tissue (5). CL regression as reflected by a decline in peripheral progesterone levels begins on day 9 of PS in rats lacking DCRs and on day 16 in decidua bearing rats (6). The present study was undertaken to determine whether the presence of decidual tissue in hamsters has any effect on ovarian progesterone secretion near the end of PS and how declining progesterone levels at that time in decidua bearing animals correlate with the termination of luteal hyperemia.

Materials and Methods. Ninety-seven female hamsters aged 2–3 mo were maintained in constant temperature rooms with a 12L:12D lighting schedule, 2400 hr being the midpoint of the dark period. After exhibiting two successive 4-day estrous cycles, female hamsters were placed with vasectomized males on the evening of proestrus (2100 hr) and mating was observed. Eighty-three to 89 hr after sterile mating (SM) all animals were anesthetized with Nembutal. Forty-seven of the anesthetized animals were subjected at that time to bilateral uterine trauma to induce DCRs by sewing two thread loops into each uterine horn. The remaining 50 PS hamsters served as nontraumatized PS controls. Blood from control animals under Nembutal anesthesia was collected from the right ovarian vein near its confluence with the postcava either at 132, 138, 144, 150 or 156 hr after SM. Ovarian venous blood from traumatized animals under Nembutal anesthesia was collected either at 156, 162, 168, 174 or 180 hr after SM. Ovarian venous blood collection lasted from 10 to 15 min, 11 min being the most common. At the time of bleeding the left ovary was inspected for the presence of hyperemic CL. Pink CL were not adjudged hyperemic.

Serum progesterone levels were determined by a modification of a radioimmunoassay method previously described (7), excepting that progesterone extracts were not subjected to column chromatography since no significant differences were revealed between columned and uncolumned extracts during characterization of the antibody. Antibody to a progesterone-11-succinate-bovine serum albumin conjugate was supplied by Endocrine Sciences[1] and exhibited a 7% cross reaction with 17α-hydroxyprogesterone and a 0.5% cross reaction with cortisol, estrone and estradiol-17β. At a 1/12,000 dilution of antibody, 4 pg of progesterone could be distinguished from a solvent blank, 0 pg. The solvent system was composed of hexane:ethyl acetate (100:1) and this solvent extracted approximately 82% of ^{3}H-progesterone from hamster serum samples. The minimum and maximum volumes of serum extracted were 25 μl and 50 μl, respectively. Both volumes of serum were diluted to 0.5 ml with solvent extracted water prior to extraction and percent recoveries of ^{3}H-progesterone were not different for the 2 vol. The slope of the dose response curve for pooled sera from pseudopregnant hamsters was not different from the slope of the standard curve. Only the linear portion of the standard curve was

[1] Endocrine Sciences, Tarzana, CA.

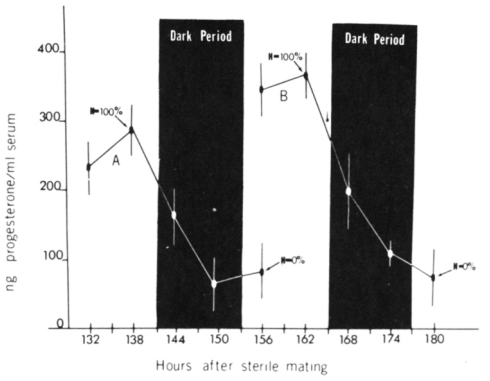

FIG. 1. Progesterone levels (ng/ml ovarian venous serum) at the indicated hrs after sterile mating in pseudopregnant hamsters without deciduomata (A) and with deciduomata (B) and maintained on a 12L:12D lighting schedule in which the dark period ended at 0600 hr. Each point represents a mean of 10 animals except those at 174 and 180 hr after sterile mating, which represent means of eight and nine animals, respectively. H equals the percent of hamsters exhibiting hyperemic corpora lutea in the left ovary at the indicated hour.

used in determining hormone concentration. This RIA technique involves the separation of antibody bound ^{3}H-progesterone from free ^{3}H-progesterone by using ammonium sulfate. Nonspecific precipitation was less than 6% of total radioactivity in each tube and zero tubes bound approximately 55% of total radioactivity.

A least squares analysis of variance was conducted to determine the effect of DCRs on progesterone secretion, the effect of time on progesterone secretion, and the interaction of the decidua effect and time on the patterns of progesterone secretion.

Results. The presence of DCRs delayed the onset of decline in progesterone secretion in PS hamsters (Fig. 1). Progesterone levels in PS hamsters with DCRs at 156 hr after SM were significantly higher ($P < 0.01$) than those in hamsters without DCRs at the same hr. In both groups the onset of luteal regression occurred overnight as evidenced by highly significant ($P < 0.01$) decreases in ovarian venous progesterone levels and disappearance of hyperemia of CL by 0900 hr of the following morning. The onset of luteal regression in hamsters with DCRs as measured by the termination of hyperemia and decrease in progesterone secretion occurred 24 hr later than in controls. Also, during the hours immediately preceding luteal regression the mean progesterone level in hamsters with DCRs was significantly higher ($P < 0.01$) than that in hamsters lacking DCRs.

Discussion. The delayed onset of decline in ovarian progesterone secretion in PS hamsters bearing decidual tissue indicates a possible antiluteolytic effect of decidual tissue. A similar effect has been reported in rats (6, 8, 9). Since prostaglandin $F_{2\alpha}$ has vasoconstrictive properties (10) and is luteolytic in hamsters (11, 12), sustained secretion of progesterone and persistence of hyperemic CL in hamsters with DCRs may be due to inhibition of the synthesis, release, or action of prostaglandin $F_{2\alpha}$ or other vasoconstrictive-luteolytic factors at the time that luteolysis would have occurred in the absence of DCRs.

That ovarian progesterone levels were significantly higher in PS hamsters with DCRs before any decline of secretion in the two groups and that elevated progesterone levels persisted 24 hr longer than PS controls suggests that the presence of DCRs may have promoted progesterone secretion. A decidual tissue luteotrophic hormone which sustains progesterone secretion has been suggested in PS rats with DCRs (13). Whether decidual tissue produces a substance promoting luteal progesterone production or augmenting secretion or action of luteotropin(s) on CL was not revealed in this investigation.

Not all hyperemic CL may be equally functional since low progesterone levels were recorded in some hamsters with hyperemic CL. That low progesterone levels were the result of methodologic problems during collection of ovarian venous blood can be ruled out since peripheral levels of progesterone reflected the same pattern (unpublished data). Low progesterone levels in PS hamsters with hyperemic CL indicate separation of the vasoconstrictive and antisteroidogenic actions of luteolytic agents in these hamsters.

Summary. Decidual tissue in pseudopregnant hamsters prolonged ovarian progesterone release by one full day. The terminal decline in circulating progesterone occurred abruptly overnight in experimental and control animals and was synchronous with termination of hyperemia. During the hours immediately preceding luteal regression the mean progesterone level was significantly higher in hamsters with decidual tissue.

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