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Serum Progesterone Levels in Hysterectomized Pseudopregnant Rabbits[1] (37766)

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The effect of hysterectomy on survival of corpora lutea (CL) differs with the species and the time at which the uterus is removed (1–4). In the guinea pig, hysterectomy on Day 4 to 6 of the estrous cycle can delay the next estrus for more than 120 days (5), although luteal progesterone concentration is decreased by 50 days (6). Removal of the uterus extends pseudopregnancy from 9 to 18 days in hamsters (7) and prolongs pseudopregnancy in rats by about 6 days (2). In humans, hysterectomy has no effect on the menstrual cycle (8), and in rabbits, which do not cycle, the effect of hysterectomy seems to depend upon the time at which the uterus is removed (3).

Hysterectomy in the pseudopregnant rabbit reportedly extends the lifespan of the CL for 6–10 days beyond their normal 15- to 17-day survival period (9, 10). In the present study, the effect of hysterectomy on the CL in pseudopregnant rabbits was evaluated by radioimmunoassay of peripheral serum progesterone.

Materials and Methods. Under pentobarbital anesthesia (approximately 25 mg/kg iv) and using a ventral surgical approach, the uterus, tubes, and cervices were removed from seven rabbits and the fallopian tubes were bilaterally ligated and cut to prevent pregnancy in five others. Five weeks later, ovulation was induced by mating with fertile bucks. One of the tube-ligated and one of the hysterectomized rabbits failed to survive throughout the experiment, both dying from pneumonia.

Blood samples for assays of serum progesterone were obtained by heart puncture prior to mating and at 3-day intervals for 30 days after mating. Serum progesterone levels were determined by radioimmunoassay (11). Ovulation was ascertained by laparotomy between Day 6 and Day 7 after copulation.

Results and Discussion. Serum progesterone. Figure 1 shows peripheral serum progesterone levels in control (tube-ligated) and hysterectomized, pseudopregnant rabbits. Because of considerable variation between individual animals, standard errors of the means are large. In both groups, the highest progesterone levels occurred on Day 9 when the mean serum progesterone of the controls was 12.0 ± 1.9 ng/ml and that of the hysterectomized animal was 11.3 ± 2.8 ng/ml. There was no significant difference between the progesterone levels of the two groups until Day 15 which normally marks the end of pseudopregnancy in the doe. At this time the serum progesterone of the control animals had fallen to about 4 ng/ml, whereas serum progesterone in the hysterectomized animals remained around 10 ng/ml. Higher levels of progesterone were sustained in the hysterectomized group in spite of a lower mean number of CL (M ± SE = 6.3 ± 1.0 vs 9.6 ± 0.7) which could be attributed to adhesions around the ovary resulting from the surgical trauma associated with tubectomy.

Our results fully confirm the early work of Asdell and Hammond (12) by showing the functional survival of the CL 6–10 days be-

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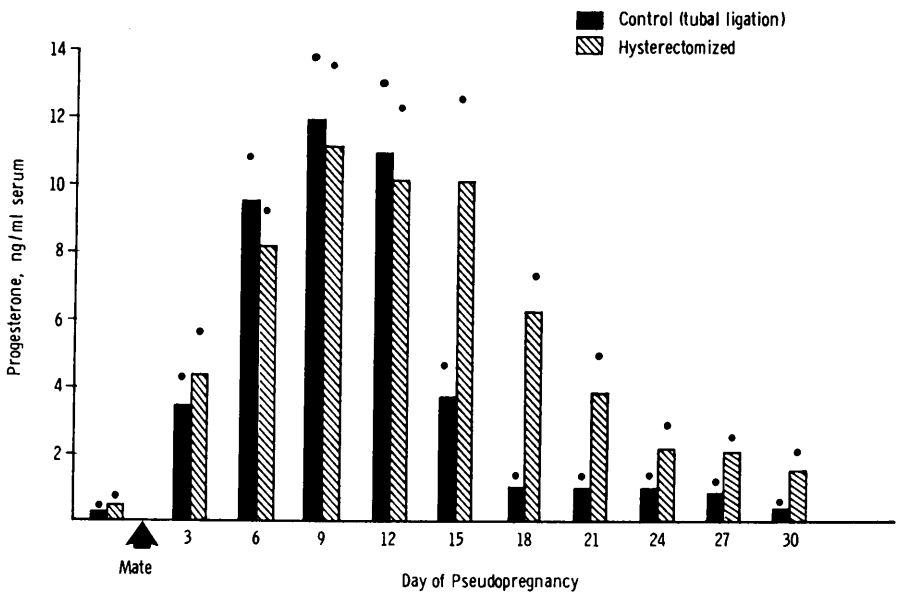

FIG. 1. Progesterone levels in the peripheral serum of pseudopregnant control and hysterectomized rabbits. Blood samples for radioimmunoassay of progesterone were collected by heart puncture. Control rabbits had had fallopian tubes ligated to prevent pregnancy. Bars and dots = M ± SE.

yond the normal 14- to 16-days pseudopregnant period. Whether this can be attributed to the removal of a uterine luteolysin or the estrogen-"sparing" effect of total hysterectomy, as first proposed by Heckel (13), is still debatable.

Scott and Rennie (14) transferred 2-day CL from donor rabbits to the kidney capsule of recipient rabbits. In estrous recipients, the CL had a lifespan of approximately 17 days, but when the CL were transferred to 12-day pseudopregnant rabbits their lifespan was reduced to about 11 days and both the ovarian and the transferred CL regressed at about the same time. Hysterectomy at the time of transfer prolonged the lifespan of both sets of CL to 23–27 days, but the CL regressed early when prostaglandin F_{2a} was given. These results, as well as ours, suggest that the endometrium of the pseudopregnant rabbit may begin to release a uterine luteolysin —possibly prostaglandin F_{2a}—about Day 12.

However, a local luteolytic action of the uterus, as in the guinea pig, hamster, and rat (15), has not been demonstrated in the rabbit. Caldwell, Mazer, and Wright (16) found that, whereas transplants of hamster or rat uterus to the cheek pouch reduced the length of pseudopregnancy in hysterectomized hamsters from 18 to 13.5 days, transplants of 14-day pseudopregnancy rabbit uterus gave inconclusive results and human endometrium was ineffective. This would suggest that if the nongravid rabbit uterus does release a luteolytic factor, it is either very weak or discharged very slowly.

On the other hand, since estrogen is clearly established as the ultimate luteotrophin in the rabbit, our results could just as well be interpreted as due to the estrogen-"sparing" effect of hysterectomy.

Summary. The effect of hysterectomy on luteal function was evaluated in 12 pseudopregnant rabbits by radioimmunoassay of progesterone in peripheral serum. Blood for assays was obtained by heart puncture before mating and on every third day of pseudopregnancy thereafter. Between Days 12 and 15, serum progesterone levels of the five controls fell sharply (M ± SE = 3.7 ± 1.0 ng/ml), whereas those of the seven hysterectomized animals remained higher (M ± SE = 10.1 ± 2.6 ng/ml). These findings are

compatible either with a uterine luteolysin in the rabbit or with an "estrogen-sparing" effect of hysterectomy.

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