— Note —

Changes in Plasma Progesterone Levels during the Estrous Cycle and Pregnancy in 4-day Cyclic Mice

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Changes in plasma progesterone levels during the estrous cycle and pregnancy were determined in group-housed IVCS strain mice showing regular 4-day cycles in the absence of a male. The pattern of progesterone secretion during the estrous cycle consisted of a large peak and a small one, the former during the late afternoon of proestrus and the latter on the afternoon of metestrus. From Day 0 to Day 2 of pregnancy, a sharp rise was observed, and then this level reached a plateau. A marked increase in progesterone was shown from Day 13 until the day before parturition.

The estrous cycle of laboratory mice has been reported to be influenced by the presence or absence of a male [5, 8, 10]. Absence of a male results in an irregular cycle and/or persistent diestrus. Nobunaga [4] showed that IVCS strain mice, even those housed in a group, exhibit the regularly repeated 4-day estrous cycle in the absence of a male. In the present study, we measured the plasma concentration of progesterone during the estrous cycle and pregnancy in this strain of mice which show the regular 4-day cycles.

A total of 278 virgin female mice (8–12 weeks old) of strain IVCS, bred in our laboratory and showing almost regular 4-day estrous cycles, were used. They were kept in a room at a temperature of 23–25 °C and exposed to a light-schedule of 14 h light and 10 h darkness (lights on at 0500 h). They received standard laboratory diet and tap water *ad libitum*.

After two consecutive 4-day estrous cycles were detected by vaginal smears, the females

were assigned to either a cyclic group or a mated (pregnant) group, and times of autopsy were randomly assigned (4–9 animals per time period). On the evening of proestrus, females of the mated group were caged overnight with mature male mice and were inspected for the presence of vaginal plugs on the following morning (Day 0 of pregnancy). Cyclic females were killed at 2 to 4-h intervals throughout the 24-h period from 0900 on the proestrus day through 0900 on the estrus and 2100 on the estrus days, and on a similar time schedule from metestrus to diestrus. Pregnant females were killed at daily intervals from Day 0 to Day 19 (day of parturition). Individual blood samples were collected from the vena cava caudalis with a heparinized syringe under ether anesthesia between 0900 and 1000 h. Plasma levels of progesterone were determined by radioimmunoassay by the procedure described previously [6]. The coefficient of variation for intra- and interassay variability were 6.0 and

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Fig. 1. Plasma progesterone levels during the estrous cycle in the mouse. Values are the mean $\pm$ SE with the number of replicates. The black bars represent the dark period (1900-0500 h) and the dashed lines denote midnight

Fig. 2. Plasma progesterone levels during pregnancy in the mouse. Values are the mean $\pm$ SE with the number of replicates

12.6%, respectively.

The pattern of progesterone secretion during the estrous cycle is shown in Fig. 1. During the afternoon of proestrus, the progesterone concentration rose to a peak of 55.5 ± 7.6 ng/ml

(mean $\pm$ SE) at 1900 h. This increase over the baseline level was significant ($p < 0.01$). After 1900 h, the progesterone levels began to decrease, falling to the baseline value by 0500 h on the day of estrus. The second significant

increase ($p < 0.01$) occurred at 1300 h of the metestrus. In these animals, no females had been found to have ovulated when they were examined at 0100 h, and all 7 females had ovulated by 0500 h. The large proestrus peak of progesterone secretion shown here is similar to that which has long been known to occur in the rat [7] and found in mice housed in the presence of a male [5] and in mice of a random-bred stock derived from a 4-way cross, Line C [2]. It was interesting that the increase in progesterone seen in metestrus was less than that in rats and Line C mice.

Fig. 2 shows the plasma concentrations of progesterone during pregnancy. From Day 0 to Day 2 of pregnancy, there was a sharp and significant increase ($p < 0.01$) to a level which was maintained with some variations until Day 12. On Day 13 the progesterone level increased again. On Day 14 and Day 17 two peak levels, 34.9 ± 4.4 and 35.2 ± 4.7 ng/mL, were found. The concentration on Day 18 was significantly less ($p < 0.01$) than that on Day 17, and this level was further decreased on Day 19 (day of parturition). There were similar progesterone patterns in our results and in previous studies [1, 3, 9] which showed a

marked increase from midpregnancy until just before parturition.

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4日性周期マウスにおける性周期中および妊娠期間中の 血漿中プロジェステロン濃度変化

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雄の近接なくして規則的な4日性周期を回帰する群飼育のIVCS系マウスを用い、性周期中および妊娠期間中の血漿中プロジェステロン濃度の変化を検討した。性周期中のプロジェステロン分泌パターンは、発情前期の午後遅くにみられる大きなピークと発情後期の午後

にみられる小さなピークの2つより構成された。妊娠期間中のプロジェステロン濃度では、妊娠0日目より2日目にかけて急激な上昇がみられ、その後はほぼ平坦な値を維持した。また、妊娠13日目より分娩日の前日まで顕著な増加が認められた。