CHANGES IN PITUITARY FSH AND LH AND PLASMA LH IN IMMATURE RATS TREATED WITH PREGNANT MARE'S SERUM

By

Shao-Yao Ying* and Roland K. Meyer

ABSTRACT

The concentrations of LH and FSH in the pituitary gland and LH in the plasma from immature rats treated with saline, 3 IU, or 12 IU PMS were measured for 4 days. There was no detectable LH in 1.5 ml of plasma at any time in saline-treated rats. In 3 IU PMS rats, an elevation was observed at 3.00 p.m. and 8.00 p.m. on day 24. The plasma LH level of 12 IU PHS rats was much higher than that of 3 IU PMS rats, reaching a maximum at 10.00 a.m. on day 23, then gradually decreasing until the morning of day 25. The pituitary FSH content in 3 IU PMS rats reached a maximum at 10.00 a.m. on day 24, then drastically decreased at 3.00 p.m. and 8.00 p.m. The pituitary FSH content of 12 IU PMS rats showed a gradual decrease without an acute release on the afternoon of day 24. These results indicate that FSH, like LH, is released on the afternoon of day 24 and may be involved in ovulation. The failure of 12 IU PMS rats to ovulate is probably due to (a) interference in the timing of ovulating hormone (OH) release, (b) lack of a surge of LH, or (c) improper ratio of LH to FSH.

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It has been reported that a single injection of pregnant mare's serum (PMS) in immature female rats causes ovulation (Cole 1937). Experiments conducted with barbiturates or other neuropharmacological drugs, and hypophysectomy (Barraclough & Sawyer 1955; Everett & Sawyer 1949; Everett et al. 1949; McCormack & Meyer 1962; Strauss & Meyer 1962; Zarrow & Quinn 1963) have shown that the release of ovulating hormone (OH) which occurs between 2:00 and 4:00 p.m. on the day of pro-oestrus in adult rats or the second day after PMS injection in immature rats depends on a neurohumoral activation of the pituitary gland.

Recent observations in this laboratory showed that the incidence of ovulation in 22-day-old rats treated with various doses of PMS reached a maximum at 3 and 30 IU, whereas 12 or 15 IU did not induce ovulation (Ying & Meyer 1969a). Furthermore, the effects of progesterone or other steroids, phenobarbital or other pharmacological drugs, and copulation on ovulation in PMS-treated immature rats approximated the effects which were previously reported for the adult (Ying & Meyer 1969b, d).

Previous studies have shown that pituitary LH is highest on the morning of pro-oestrus and decreased during the critical period, reaching minimal values on the morning of oestrus (Mills & Schwartz 1961; Schwartz & Bartosik 1962), while plasma LH levels have been shown to increase during the afternoon of pro-oestrus (Ramirez & McCann 1963; Schwartz & Calderelli 1965). These observations support the existence of the "critical period" reported by Everett et al. (1949).

In addition, changes in pituitary and plasma FSH similar to the fluctuation of LH levels during pro-oestrus and oestrus were reported (Mills & Schwartz 1961; Schwartz & Bartosik 1962). Pituitary FSH content, as measured by the Steelman-Pohley assay (Steelman & Pohley 1953) was elevated at 10:00 a.m. on the day of pro-oestrus in rats exhibiting 4- and 5-day cycles. The FSH content decreased to minimal values by 3:30 p.m. on that day, coinciding with an increase of FSH in the plasma. Both pituitary and plasma FSH were low during oestrus. A recent report of Goldman & Mahesh (1968) suggested a prominent role of "acute-released-FSH" approximately concurrently with the ovulatory surge of LH during the pro-oestrus critical period in the rat. Quantitative bioassay of LH and FSH in pituitary glands removed during the afternoon of the day preceding PMS-induced ovulation in immature rats showed no change in LH, but a 32% decrease in pituitary FSH was noted (Rennels & O'Steen 1967).

In the present experiment we used the modification of the ovarian ascorbic acid depletion (OAAD) method described by Bogdanove & Gay (1967) to measure pituitary and plasma levels of LH and the HCG-augmentation method of Steelman & Pohley (1953) to measure pituitary FSH levels in immature female rats treated with PMS.
MATERIALS AND METHODS

Donor rats. – Twenty-one-day-old female rats weighing 45–50 g were received from the Badger Research Corp., Madison, Wisconsin. The rats were maintained on Rockland rat chow and water ad libitum and were exposed to 14 hours of light and 10 hours of darkness at a room temperature of 24–28°C. All times mentioned in this report are »colony time«. In this convention of Everett & Sawyer (1950) midnight, Colony Time, is the middle of the dark period. Animals were divided into three groups. One group received a subcutaneous injection of 0.25 ml saline, the other two received 3 or 12 IU PMS Equinex® (Ayerst Laboratories, Chicago) in 0.25 ml saline on day 22 between 7:00 and 8:00 a.m. At 10:00 a.m. on days 22, 23, and 24, 3:00 p.m. and 8:00 p.m. on day 24; and 9:00 a.m. of day 25, six to eight rats from each group were anaesthetized with ether and bled from the posterior vena cava into a heparinized syringe with 18 gauge needle. Blood was pooled and centrifuged.

The animals were killed immediately after blood collection. The pituitary glands were removed, the neurohypophyses were discarded and the adenohypophyses were placed in 0.5 ml saline and frozen on dry ice as quickly as possible. The frozen pituitaries within each treatment group were pooled and stored at -20°C until assayed in 2 weeks; each pool contained from 5–8 pituitaries. At the time of use the pituitaries were thawed, homogenized in a ground glass tube in physiological saline to a concentration of 1 pituitary per ml. A volume of 0.01 pit./0.01 ml of the suspension for each pool was saved for the bioassay of pituitary LH, the rest was adjusted to the proper concentration for FSH determination.

FSH-determination

A modified Steelman-Pohley assay (Steelman & Pohley 1953) was used to determine pituitary FSH potency. Female rats weighing 45–50 g were obtained from the Holtzman Rat Company at 21 days of age. The light, temperature and food were identical to that described above for the donor rats. Subcutaneous injections of test material were given twice daily in the morning and afternoon of days 22, 23, and 24. The homogenized pituitaries were suspended in saline and combined with 50 IU HCG (International Hormones, Hicksville, L.I., New York) so that each assay animal received a total dose of 3.0 ml or 0.5 ml per injection. On day 25 the rats were sacrificed and the ovaries removed and weighed. Relative potencies were calculated according to the method of Bliss (1952).

LH-determination

Twenty-three-day-old female rats weighing from 65–70 g were obtained from the Holtzman Rat Company. The maintenance of the animals was the same as described above for the donors. A subcutaneous injection of 50 IU PMS in 0.5 ml saline was given between 10:00 and 11:00 a.m. on day 25, and 25 IU HCG in 0.5 ml saline was given subcutaneously between 4:00 and 5:00 p.m. on day 27. The animals received daily subcutaneous injections of 10 µg of oestradiol-3-benzoate in 0.1 ml of corn oil from day 30 through day 38. The assay was performed when the rats were 39 days of age, using the »2 ovary« method described by Bogdanove & Gay (1967). The right ovary was removed and 1.0 or 1.5 ml of the assay material was injected intravenously. The animals were sacrificed by cervical dislocation two hours ± 2 min later, when the left ovary was removed. The concentration of ascorbic acid was determined by the method of Mindlin & Butler (1938). The percentage of ovarian ascorbic acid depletion

222
Table 1.
Plasma LH during days 22 to 25 in immature rats treated with 3 or 12 IU PMS on the 22nd day of life (1.5 ml plasma).

<table>
<thead>
<tr>
<th>Time of plasma collection</th>
<th>Per cent ascorbic acid depletion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Saline control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>10:00 a.m., day 22</td>
<td>1.59 ± 1.30**</td>
<td>A,C; &lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>10:00 a.m., day 23</td>
<td>1.13 ± 0.43**</td>
<td>A,C; &lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>10:00 a.m., day 24</td>
<td>1.49 ± 0.93**</td>
<td>A,C; &lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td></td>
</tr>
<tr>
<td>3:00 p.m., day 24</td>
<td>5.32 ± 0.34**</td>
<td>A,B; &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>(4)</td>
<td></td>
</tr>
<tr>
<td>8:00 p.m., day 24</td>
<td>0.57 ± 1.01**</td>
<td>A,B; &lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td></td>
</tr>
<tr>
<td>9:00 a.m., day 25</td>
<td>0.38 ± 1.01</td>
<td>A,C; &lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td></td>
</tr>
</tbody>
</table>

* OAAD % is expressed as mean±se (No. of test rats).
** Repletion.
(a) Significantly different from groups 1, 2, 3, and 6.
(b) Significantly different from groups 1, 3, 4, 5, and 6.

was measured on the same day for both experimental and control pituitaries and plasma to eliminate day-to-day variations in sensitivity of the rat. Significance of the differences between the 2 groups was calculated by Duncan's multiple range test (Duncan 1955).

RESULTS

The results of the assays are presented in Tables 1, 2 and 3.

Plasma LH activity

No detectable LH was found in 1.5 ml of plasma collected on days 22–25 from immature rats treated with saline. In immature rats treated with 3 IU PMS, the only detectable LH was found in plasma collected at 3:00 p.m. and 8:00 p.m. on day 24. Plasma from immature rats treated with 12 IU PMS
Table 2.
Pituitary LH during days 22 to 25 in immature rats treated with 3 or 12 IU PMS on the 22nd day of life (0.01 pit./1.0 ml).

<table>
<thead>
<tr>
<th>Time of pituitary removal</th>
<th>Per cent ascorbic acid depletion</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Saline control (A)</td>
<td>3 IU PMS (B)</td>
</tr>
<tr>
<td><strong>10:00 a.m., day 22</strong></td>
<td>19.36±1.02 (6)</td>
<td>17.64±1.29 (5)</td>
</tr>
<tr>
<td><strong>10:00 a.m., day 23</strong></td>
<td>17.85±2.69 (6)</td>
<td>20.17±2.20 (4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>10:00 a.m., day 24</strong></td>
<td>15.08±0.37 (5)</td>
<td>33.86±6.54 (6)</td>
</tr>
<tr>
<td><strong>3:00 p.m., day 24</strong></td>
<td>17.71±1.51 (5)</td>
<td>26.04±3.37 (6)</td>
</tr>
<tr>
<td><strong>8:00 p.m., day 24</strong></td>
<td>28.01±1.36(a) (5)</td>
<td>21.94±3.18 (6)</td>
</tr>
<tr>
<td><strong>9:00 a.m., day 25</strong></td>
<td>24.55±4.12 (4)</td>
<td>17.23±1.45 (6)</td>
</tr>
</tbody>
</table>

* OAAD % is expressed as mean±se (No. of test rats).
(a) Significantly different from groups 1, 2, 3, and 4.
(b) Significantly different from groups 1, 2, 5, and 6.

The values at these times were not significantly different from one another but were less than that found on the morning of day 23. In the experiment reported above, 1.5 ml aliquots of pools of plasma collected at given time periods of days 22–25 from saline, 3 or 12 IU PMS-treated rats were tested. LH standard was run concurrently at two dose levels against a 1.5 ml dose of plasma. The results of these assays are given in Table 1.

Pituitary LH activity
Each pituitary collected at a different time on days 22–25 was tested for ovarian ascorbic acid depletion ability with concurrent LH standard and saline
Table 3.
Pituitary FSH during days 22 to 25 in immature rats treated with 3 or 12 IU PMS on the 22nd day of life.

<table>
<thead>
<tr>
<th>Time of pituitary removal</th>
<th>FSH/gland</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Saline control (A)</td>
<td>3 IU PMS (B)</td>
<td>12 IU PMS (C)</td>
</tr>
<tr>
<td>10:00 a.m., day 22</td>
<td>152.5* (147.3–169.6)</td>
<td>(121.4–153.6)</td>
<td>128.0 (110.2–137.4)</td>
</tr>
<tr>
<td>10:00 a.m., day 23</td>
<td>139.2 (125.1–147.6)</td>
<td>145.4 (146.2–161.3)</td>
<td>129.0 (117.6–131.5)</td>
</tr>
<tr>
<td>10:00 a.m., day 24</td>
<td>126.1 (113.7–132.3)</td>
<td>172.8 (146.9–189.4)</td>
<td>117.1 (89.3–131.7)</td>
</tr>
<tr>
<td>3:00 p.m., day 24</td>
<td>123.2 (115.6–130.2)</td>
<td>110.4(b) (98.3–127.5)</td>
<td>94.5 (74.5–126.8)</td>
</tr>
<tr>
<td>8:00 p.m., day 24</td>
<td>122.8 (101.5–129.8)</td>
<td>67.4(b) (49.0–74.4)</td>
<td>89.8 (70.9–102.9)</td>
</tr>
<tr>
<td>9:00 a.m., day 25</td>
<td>112.6 (101.4–123.8)</td>
<td>45.8 (38.5–52.4)</td>
<td>69.1 (58.8–76.2)</td>
</tr>
</tbody>
</table>

* Mean (95% confidence limits).
Poled regression and lambda were 673.13 and 0.089, respectively.
FSH/gland is expressed as µg equivalents of NIH-FSH-S3.
(a) Significantly different from each other.
(b) Significantly different from each other.

Injection control in two assays. The method was sufficiently sensitive to detect LH in as little as one hundredth of an immature rat pituitary gland weighing approximately 3 mg. The results are summarized in Table 2. There was a slight but consistent decrease in pituitary LH activity from day 22 to day 24 in immature rats given saline on day 22, but the pituitary LH content increased significantly at 8:00 p.m. on day 24 and at 9:00 a.m. on day 25. Following administration of 3 IU PMS on day 22, pituitary LH rose significantly, reached a peak at 10:00 a.m. on day 24 and then decreased steadily through day 25. Lowest pituitary LH was found at 9:00 a.m. on day 25 in 3 IU PMS-treated rats.

Pituitary LH content of 12 IU PMS-treated immature rats rose to a peak at 10:00 a.m. on day 23, decreased at 10:00 a.m. and 3:00 p.m. on day 24, then increased at 8:00 p.m. on day 24 and 9:00 a.m. on day 25.
Pituitary FSH content

Pituitary FSH levels (Table 3) in saline-treated immature rats showed a slight decrease at 10:00 a.m. on days 22, 23 and 24 (152.5 µg, 139.2 µg and 126.1 µg FSH/pituitary, respectively). The values from pituitaries collected on day 24 and the morning of day 25 changed very little (from 126.1 µg to 112.6 µg per pituitary). The FSH level in 3 IU PMS-treated rats at 10:00 a.m. on day 22 was 135.6 µg/pituitary, showed an increase at 10:00 a.m. on day 23 (145.4 µg/pituitary) and a further increase to very high levels (172.8 µg/pituitary at 10:00 a.m. on day 24, drastically decreased to 110.4 µg at 3:00 p.m. and to 67.4 µg at 8:00 p.m. on day 24. A further but slight decrease was observed at 9:00 a.m. on day 25. The hypophyseal FSH of 12 IU PMS-treated rats at 10:00 a.m. on day 22 was 128.0 µg/pituitary, 123.0 µg at 10:00 a.m. on day 23 and slightly decreased at 10:00 a.m. on day 24 (117.1 µg/pituitary). There were two decreases of pituitary FSH in 12 IU PMS-treated immature rats: one at 3:00 p.m. on day 24 (from 117.1 µg to 94.5 µg), the other on the morning of day 25 (from 89.9 µg to 69.1 µg).

DISCUSSION

The results demonstrate that changes in pituitary gonadotrophin content and plasma LH levels in immature rats treated with 3 or 12 IU of PMS are correlated with the presence or absence of ova in the oviducts. This suggests that timed endogenous gonadotrophin secretion may play an important role in the process of ovulation induced by administration of PMS. A slight but consistent decrease in pituitary FSH and undetectable plasma LH from day 22 to day 25 in saline-treated immature rats agree with previous findings reported by Kragt & Ganong (1967) and Ramirez & McCann (1963). The gradual decrease in pituitary LH from day 22 to 10:00 a.m. on day 24 was similar to a previous observation reported by Lisk (1967). However, the pituitary LH increased at 8:00 p.m. on day 24, probably due to diurnal fluctuations.

It is of interest to note that in 3 IU PMS-treated rats, pituitary LH increased at 10:00 a.m. on day 24, and then steadily decreased through day 25. Plasma LH, which was not detectable at 10:00 a.m. on days 22, 23, 24 and at 9:00 a.m. on day 25, was increased at 3:00 and 8:00 p.m. on day 24. These gonadotrophin fluctuations in the pituitary and circulating LH are similar to those observed in cyclic female rats by McCann et al. (1967), Anderson & McShan (1964) and Schwartz (1964), and indicate that a considerable excess of LH is released during the critical period which is well above the minimal ovulation quota. The administration of 3 IU PMS to immature rats has been reported to induce 80% of the animals to shed an average of 5 ova (Ying & Meyer 1969a). Furthermore, the increase in pituitary FSH up to 10:00 a.m. on day 24 fol-
ollowed by the decrease through day 25, indicates release of FSH as well as LH during the critical period in 3 IU PMS-treated rats. This result agrees with similar findings in cyclic adult rats reported by Caligaris et al. (1967) and Goldman & Mahesh (1968), and PMS-treated immature rats reported by Rennels & O'Steen (1967).

It has been shown that properly timed hypophysectomy (Everett 1956) or barbiturate administration (Everett & Sawyer 1950; Everett 1956) on the afternoon of pro-oestrus will prevent ovulation in adult rats, presumably by preventing the release of hypophyseal LH. Subsequently, it was shown that pituitary LH content decreased (Schwartz & Bartosik 1962; Schwartz & Calderelli 1965) and plasma LH concentration increased (Ramirez & McCann 1963; Schwartz & Calderelli 1965; Anderson & McShan 1964) on the afternoon of pro-oestrus. Ovulation in the PMS-treated immature rat has been shown to be dependent on the release of OH from the pituitary gland during the afternoon of the day preceding ovulation (McCormack & Meyer 1962; Strauss & Meyer 1962; Zarrow & Quinn 1963). Rennels & O'Steen (1967) found that no change in pituitary LH occurred between 2:00 and 7:00 p.m., but that there was a 32% decrease in pituitary FSH on the day preceding ovulation. The results presented indicate that the only detectable LH was found in plasma collected at 3:00 p.m. and 8:00 p.m. on day 24 in 3 IU PMS rats. These detectable plasma peaks followed a pituitary LH peak at 10:00 a.m. on day 24 followed by a steady decline. Goldman & Mahesh (1968) reported that a decrease in hypophyseal LH and FSH was found to occur in pubertal rats on the day preceding their first ovulation, and the LH level had fallen still lower at oestrus. Rennels & O'Steen (1967) were unable to detect LH plasma from PMS-treated immature rats during the afternoon of the day preceding ovulation, possibly due to the insensitivity of the assay method they used. The OAAD method modified by Bogdanove & Gay (1967) has been reported 5 to 9 times more sensitive than the original OAAD assay. However, some earlier investigators using bioassay techniques found elevated plasma LH on the morning and afternoon of pro-oestrus in adult cycling rats (Ramirez & McCann 1963; Schwartz & Calderelli 1965; Anderson & McShan 1964). These differences may be attributed to the lack of sensitivity of bioassay techniques. Because of the low concentration of plasma LH, many measurements made at the lower limits of bioassay sensitivity may be less reliable than measurements made at higher concentrations of LH.

During the preparation of this manuscript, Monroe et al. (1969), using a radioimmunoassay, reported that the plasma LH in cycling adult rats elevated as early as 1:00 p.m. and as late as 8:00 p.m. on the afternoon of pro-oestrus, but the highest incidence of elevated concentrations was observed between 3:00 and 6:00 p.m. No significant elevation in plasma LH was observed during the afternoon of dioestrus. If the results of our pituitary and plasma LH
measurements are examined on a similar basis, the time of highest plasma LH in 3 IU PMS rats is surprisingly similar to that in adult cycling rats.

Previous study (Ying & Meyer 1969a) in this laboratory showed that ovulation with an average of 5 ova occurred in over 80% of 25-day-old rats given a single injection of 3 IU PMS at 22 days of age. However, 12 or 15 IU PMS only occasionally produced ovulation in the same animals under the same regimen. A higher plasma LH in 12 IU PMS rats than in 3 IU PMS rats was different from what we had anticipated. The plasma collected at 10:00 a.m. on day 22 from immature rats treated with 12 IU PMS gave significant ascorbic acid depletion but there was no significant decrease in pituitary LH. The highest plasma LH of 12 IU PMS rats was observed at 10:00 a.m. on day 23, accompanied by a pituitary LH elevation. Unpublished data in this laboratory showed that as little as 0.1 IU of PMS caused a positive response in the OAAD method described by Bogdanove & Gay (1967), owing to the inherent LH activity of PMS. The half life of PMS in the rat has been determined as 26 hours (Parlow 1961). These results indicate that the plasma LH peak at 10:00 a.m. on day 23 may be the effect of both endogenous LH and the inherent LH activity of circulating PMS.

The results presented here indicate that the pituitary FSH content in 3 IU PMS rats reached a maximum at 10:00 a.m. on day 24, drastically decreased at 3:00 p.m. and 8:00 p.m. on day 24. These decreases in pituitary content also coincided with the highest plasma LH at 3:00 and 8:00 p.m. on day 24. However, pituitary FSH content of 12 IU PMS rats gradually decreased on the afternoon of day 24. These results indicate that FSH, like LH, is released on the afternoon of the day preceding ovulation in 3 IU PMS rats. This release of both FSH and LH is responsible for ovulation. Our data agree with the observation of Goldman & Mahesh (1968) that a sharp decrease in pituitary FSH occurred at approximately the same time as the pro-oestrus drop in LH in adult female rats.

Because of insensitivity of the HCG-augmentation method for assaying FSH in plasma of immature rats, we measured pituitary FSH content only with the assumption that the decline in pituitary FSH reflects the release of FSH into the blood. Ovulation has been obtained with purified FSH in hypophysectomized rats, providing the follicles were prepared with both FSH and LH. Intravenous injection of 50 μg FSH after phenobarbital block of ovulation restored the incidence of ovulation in PMS-treated immature rats (unpublished data). Goldman & Mahesh (1968) demonstrated that PMS-primed rats could be ovulated readily with the FSH alone. Experiments utilizing gonadotrophin antisera (Goldman & Mahesh 1969) further clarified the role of FSH during the pro-oestrous critical period for ovulation in the adult hamster.

Klausing & Meyer (1968) have reported that ovulating hormone in the pituitary decreased during the critical period, 2:00 to 4:00 p.m. on the day pre-
ceeding ovulation, and was minimal in the morning after ovulation in PMS-primed rats, as determined by ovulating hormone assay. Comparing the data of gonadotrophin levels in both 3 and 12 IU PMS rats, we suggest that OH is probably a combination of LH and FSH. The simultaneous release of FSH and LH which appears to occur results in a large excess of ovulating hormone. The failure of 12 IU PMS rats to ovulate is probably not due to insensitivity of the ovaries because intravenous injection of exogenous ovulators such as LH and HCG (Zarrow et al. 1958) induce ovulation. Progesterone, deoxycorticosterone, corticosterone, 20α- or 20β-hydroxyprogesterone injected at 10:00 a.m. on day 24 also produced ovulation in 12 IU PMS rats (Ying & Meyer 1969b). Other experiments conducted in this laboratory (Ying & Meyer, in press) showed that injection of metopirone at 10:00 a.m. on day 24 in immature rats pretreated with 12 IU PMS facilitated ovulation in 75 to 92% of the animals. Measurement of pituitary LH and FSH and plasma LH in metopirone-injected animals indicated that pituitary FSH increased following a rapid decrease after the administration of metopirone and then continuously decreased from 3:00 p.m. on day 24 to the morning of day 25; pituitary LH decreased rapidly after metopirone injection, suggesting the metopirone administered 4 hours before the critical period stimulates accumulation and release of deoxycorticosterone which consequently facilitates OH release in 12 IU PMS-treated immature rats. These data indicate that the failure of ovulation in immature rats injected with 12 IU PMS is probably due to: (a) interference in the time of OH release, (b) lack of a surge of LH on the afternoon of the day preceding ovulation, or (c) improper ratio of LH to FSH.

REFERENCES


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