Correlation of growth hormone secretion during pregnancy with circulating prolactin in rats

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Growth hormone (GH) concentrations were measured throughout pregnancy in rats. The effects of surgical stress, ovariectomy, and treatments with the antiprogestosterone mifepristone (RU 486) or the anti-oestrogen tamoxifen on serum GH, progesterone and prolactin were studied. GH concentrations were low during the first 18 days of pregnancy, except on the morning of day 5, and increased progressively from day 19 reaching peak values on the mornings of days 21 and 22. Thereafter GH concentrations decreased progressively, reaching very low values at 24.00 h on day 22, in parallel with a rise in serum prolactin concentrations. Surgical stress, performed at 12.00 h on day 20 of pregnancy, diminished serum GH concentrations 10 min later, but these returned to values similar to those of the non-operated rats 1–24 h later. Surgical stress did not modify serum prolactin concentrations at any time. Ovariectomy performed on the morning of day 19 produced the expected fall in serum progesterone and a rise in prolactin which lasted until the night of day 20. Serum GH concentrations were significantly diminished with respect to controls on day 20 and the morning of day 21 and then increased. Treatment with mifepristone on day 19 produced a simultaneous rise in serum prolactin and a fall in serum progesterone and GH by 08.00 h on day 21. Treatment with tamoxifen on days 3 and 4, or given daily from day 17 onwards did not modify prolactin concentrations but diminished serum GH concentrations at 08.00 on day 5 and on days 19–22, with the exception of a peak on day 22 (08.00 h). Tamoxifen also decreased serum progesterone concentrations. These results show that pregnant rats have a reduced capacity of response to stress in terms of changes in GH and prolactin secretion. There are high serum concentrations of GH at the end of pregnancy. The regulation of GH secretion at this time is different from that of prolactin and does not seem to depend on the fall in progesterone concentrations. However, serum GH concentrations seem to be inversely correlated with serum prolactin concentrations, as they tended to fall after increases in prolactin above basal concentrations. Oestrogen may also have a stimulatory role on GH since administration of an anti-oestrogen also resulted in a fall in GH concentrations in spite of reduced prolactin secretion.

**Introduction**

Regulation of growth hormone (GH) secretion shows some similarities to and some differences from prolactin secretion. GH is secreted in an ultradian fashion as several daily peaks, and there is a marked sexual dimorphism which is caused mainly by sex steroids (Tannenbaum and Martin, 1976; Eden, 1979; Jansson et al., 1984, 1985). GH secretion is stimulated by GH-releasing hormone, inhibited by somatostatin, which also inhibits prolactin, and GH and prolactin are stimulated by oestrogens (Jansson et al., 1985; Hall et al., 1986). Glucocorticoids have dual actions on GH release and inhibit prolactin release (Leung et al., 1980; Nakagawa et al., 1987a, b). Both hormones are also modulated by neurotransmitters; serotonin is mainly stimulatory for both (Martin et al., 1978; Willoughby et al., 1987), whereas catecholamines have opposite effects on GH and prolactin secretion (Martin et al., 1978; Eden et al., 1979; Willoughby and Day, 1981; Crowley et al., 1982). Stress also has opposite effects, stimulating prolactin release and inhibiting GH (Schalch and Reichlin, 1966; Takahashi et al., 1971; Krulich et al., 1974; Terry et al., 1976; Eden, 1978). Finally, the suckling stimulus induces secretion of prolactin and GH, although the latter only in a transient manner (Sar and Meites, 1969; Saunders et al., 1976; Nagy et al., 1986).

In rats, the fall in circulating progestosterone at the end of pregnancy is followed by an increase in serum prolactin (Vermouth and Deis, 1972, 1974; Bussmann and Deis, 1979) which is

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Received 20 May 1992.
mediated by adrenergic but not serotonergic pathways (Jahn and Deis, 1987, 1988, 1991). In the present study, we investigated the circulating concentrations of GH throughout pregnancy in rats and the regulation of GH by stress and gonadal hormones. Previous studies performed on selected days of pregnancy (Saunders et al., 1976; Klindt et al., 1981; Carlsson et al., 1990) showed that there is an increase in GH secretion in the last days of pregnancy. We, therefore, studied the profile of GH secretion at different times on days 4–6, 11–13 and 18–22 of pregnancy. We also investigated whether procedures known to advance prolactin secretion through a fall in or blockade of progesterone (such as ovariectomy or treatment with the anti-progesterone mifepristone) could modify GH secretion at the end of pregnancy. In addition, we studied the effect of tamoxifen administration, as oestrogens appear to stimulate GH secretion (Simard et al., 1986; Ho et al., 1987). Some of these results have been presented in abstract form (Jahn et al., 1987).

**Materials and Methods**

**Animals**

Virgin female rats, three to four months old (200–220 g) bred in our laboratory and originally of the Wistar strain, were used. The rats were kept in a light (light on 06:00–20:00 h) and temperature (22–24°C)-controlled room; rat chow (Cargill, Buenos Aires and Nutric, Cordoba) and tap water were available ad libitum. Vaginal smears were taken daily. Rats were caged individually with fertile males on the night of proestrus, and the presence of spermatozoa was checked in the vaginal smear the following morning. This day was designated day 1 of pregnancy. In our laboratory, rats usually give birth on day 23. All the rats were handled daily, to minimize the effect of handling stress. The experiments were performed in accordance with the NIH Guide for the Care and Use of Laboratory Animals (NIH publication No. 86–23, revised 1985).

**Experimental procedures**

To study GH concentrations throughout pregnancy, serum samples were obtained after decapitation or cardiac puncture of conscious animals at 08.00, 12.00, 16.00, 20.00 and 24.00 h on days 4, 5, 6, 11, 12, 13, 18, 19, 20, 21 and 22 of pregnancy. Rats were bled once by cardiac puncture on days 4–6 or 11–13 and the second time after decapitation on days 19 to 22. All the groups sampled on days 4–6 and 11–13 included samples from decapitated rats, whose hormone concentration did not differ from the samples obtained by cardiac puncture. These samples can be considered as from unstressed rats, since they were obtained within 15 s and serum prolactin values obtained in these rats were not different from those obtained in decapitated rats from the same experimental groups. Blood was allowed to clot at room temperature; the serum was separated and stored frozen at −30°C until assayed for GH and prolactin.

**Surgical procedures**

Ovariectomy was performed through bilateral incisions under ether anaesthesia between 08.00 and 09.00 h on day 19 of pregnancy. Groups of intact or sham-operated rats were used as controls, and since the hormone concentrations of both groups did not differ, they were considered as one group for statistical evaluation and expression of results.

To determine the effect of the surgical stress on serum GH and prolactin concentrations, a group of daily handled pregnant rats were sham operated (laparotomized) at 12.00 h on day 20 of pregnancy under ether anaesthesia. Groups of rats were decapitated 10 min, 1 h, 4 h and 24 h after surgery and blood was obtained for GH and prolactin determinations. The values obtained were compared with those of intact pregnant rats obtained at the same times of day.

**Drug treatments**

Mifepristone (RU 38486, donated by Roussel-Uclaf, Romainville, France) dissolved in sunflower seed oil (2 g l⁻¹) was injected s.c. at a dose of 2 mg kg⁻¹ at 08.00 h on day 19 of pregnancy.

Tamoxifen (ICI 46474, donated by Gador, Buenos Aires) was dissolved in 0.5% Tween 80 (50 mg l⁻¹) and given per os at a dose of 0.5 mg kg⁻¹ to a group of rats at 08.00 and 18.00 h on days 3 and 4 of gestation. The rats were decapitated at 08.00 h on day 5 and trunk blood collected for hormone determinations.

For the experiments at the end of pregnancy, tamoxifen was dissolved in sunflower seed oil (1 g l⁻¹) and injected daily at a dose of 200 μg per rat at 09.00 h from day 17 of pregnancy until the morning the rats were killed.

Blood samples were obtained from groups of 8–10 animals subjected to the different treatments at 12.00, 16.00 or 20.00 h on day 19 and 08.00, 12.00, 16.00 or 20.00 h on days 20, 21 or 22. The first sample was obtained by cardiac puncture on days 19 or 20 and the second after decapitation at least 36 h later. In the mifepristone-treated rats, the last sample was obtained at 08.00 h on day 22 as by this time most of these animals had already given birth.

**Prolactin, progesterone and GH determinations**

Prolactin and GH were measured by double antibody radioimmunoassays using materials generously provided by the NIADDK (S. Raitt, NIADDK Rat Pituitary Hormone Distribution Program). The hormones were radio-iodinated using the chloramine T method and purified by passage through Sephadex G75. The results were expressed in terms of the rat prolactin RP-3 and rat GH RP-2 standard preparations. Assay sensitivity for both hormones was 0.5 ng ml⁻¹ serum and the inter- and intra-assay coefficients of variation were less than 10%.

Serum progesterone was measured using a radioimmunoassay developed in our laboratory (Bussmann and Deis, 1979) with an antiserum raised in rabbits against progesterone-11–BSA conjugate. Assay sensitivity was less than 5 ng ml⁻¹ serum and the inter- and intra-assay coefficients of variation were less than 10%.

**Statistical analysis**

Statistical analysis was performed using one- or two-way analysis of variance followed by the least significant difference
Regulation of GH during pregnancy

Fig. 1. Concentrations of growth hormone in serum during pregnancy in rats. Results are the means ± SEM of six determinations for days 4–18 and of 10–15 on days 19–22. *Significantly different ($P < 0.05$) from the means of days 4–18 (excluding day 5, 08.00 h).

Fig. 2. Effect of sham surgery (laparotomy) under ether anaesthesia performed on rats at 12.00 h on day 20 of pregnancy on serum GH and prolactin (PRL) concentrations at various times after surgery. Comparison with serum hormone concentrations in intact rats sampled at the same times. Results are expressed as means ± SEM of groups of five to six rats per sampling time. *Significantly different ($P < 0.05$) from control results.

between means test when more than two experimental groups were compared or by Duncan's multiple range test for analysis of the significance between different groups during pregnancy or after surgery (Snedecor and Cochran, 1967).

Results

Effect of surgical stress on serum GH and prolactin concentrations in pregnant rats

To ascertain the effect of surgery alone on serum GH and prolactin, groups of 5–6 rats were bled by decapitation 10 min, 1 h, 4 h and 24 h after sham surgery (laparotomy) under ether anaesthesia performed at 12.00 h on day 20 of pregnancy, when serum GH concentrations are high (Fig. 1) and compared with values for non-operated rats decapitated at the same times. Ten minutes after surgery there was a significant decrease in serum GH concentrations, whereas 1–24 h after surgery, values were not different from the non-operated group (Fig. 2). There were no significant changes in serum prolactin concentrations at any of the times studied (Fig. 2). As blood samples in the ovariectomized rats were taken from 4 h after surgery, the observed changes in serum GH and prolactin values were due to the different treatments and not to surgical stress.
**Table 1.** Serum GH, prolactin and progesterone concentrations (ng ml⁻¹) in rats on days 19–22 of pregnancy. Effects of ovariectomy, treatment with mifepristone or tamoxifen

<table>
<thead>
<tr>
<th>Day of gestation and time of day when samples were taken</th>
<th>Treatments</th>
<th>Controls</th>
<th>Ovariectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>GH</td>
<td>Prolactin</td>
</tr>
<tr>
<td><strong>Day 19</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.00 h</td>
<td>15.7 ± 1.6</td>
<td>8.0 ± 1.8</td>
<td>64.3 ± 3.1</td>
</tr>
<tr>
<td>16.00 h</td>
<td>10.8 ± 1.3</td>
<td>5.6 ± 1.0</td>
<td>55.5 ± 2.9</td>
</tr>
<tr>
<td>20.00 h</td>
<td>22.2 ± 3.1</td>
<td>3.3 ± 0.2</td>
<td>54.7 ± 4.9</td>
</tr>
<tr>
<td><strong>Day 20</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>8.00 h</td>
<td>28.0 ± 7.0</td>
<td>7.1 ± 1.2</td>
<td>62.1 ± 4.3</td>
</tr>
<tr>
<td>12.00 h</td>
<td>32.2 ± 6.0</td>
<td>6.4 ± 1.1</td>
<td>46.6 ± 3.8</td>
</tr>
<tr>
<td>16.00 h</td>
<td>27.8 ± 3.6</td>
<td>9.1 ± 0.8</td>
<td>70.3 ± 3.0</td>
</tr>
<tr>
<td>20.00 h</td>
<td>30.1 ± 4.8</td>
<td>5.8 ± 0.6</td>
<td>61.5 ± 5.6</td>
</tr>
<tr>
<td><strong>Day 21</strong></td>
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</tr>
<tr>
<td>8.00 h</td>
<td>53.0 ± 5.3</td>
<td>7.5 ± 0.5</td>
<td>58.3 ± 3.1</td>
</tr>
<tr>
<td>12.00 h</td>
<td>36.6 ± 3.3</td>
<td>5.4 ± 0.6</td>
<td>43.0 ± 4.2</td>
</tr>
<tr>
<td>16.00 h</td>
<td>42.1 ± 7.6</td>
<td>7.8 ± 0.8</td>
<td>50.0 ± 5.0</td>
</tr>
<tr>
<td>20.00 h</td>
<td>28.7 ± 2.7</td>
<td>5.7 ± 0.5</td>
<td>48.5 ± 2.2</td>
</tr>
<tr>
<td><strong>Day 22</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.00 h</td>
<td>29.2 ± 2.1</td>
<td>9.3 ± 0.4</td>
<td>41.2 ± 7.6</td>
</tr>
<tr>
<td>12.00 h</td>
<td>54.0 ± 11.0</td>
<td>15.6 ± 0.6</td>
<td>23.3 ± 4.7**</td>
</tr>
<tr>
<td>16.00 h</td>
<td>25.1 ± 3.8**</td>
<td>30.4 ± 4.5**</td>
<td>18.8 ± 2.8**</td>
</tr>
<tr>
<td>20.00 h</td>
<td>12.7 ± 1.5**</td>
<td>22.4 ± 6.4**</td>
<td>12.8 ± 2.1**</td>
</tr>
<tr>
<td><strong>Day 19</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.00 h</td>
<td>21.8 ± 1.9</td>
<td>6.6 ± 1.2</td>
<td>59.6 ± 4.3</td>
</tr>
<tr>
<td>16.00 h</td>
<td>24.0 ± 4.0*</td>
<td>3.2 ± 0.8</td>
<td>47.4 ± 2.7</td>
</tr>
<tr>
<td>20.00 h</td>
<td>16.2 ± 5.5</td>
<td>6.1 ± 0.9</td>
<td>37.5 ± 4.6</td>
</tr>
<tr>
<td><strong>Day 20</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.00 h</td>
<td>35.9 ± 6.7</td>
<td>6.9 ± 0.9</td>
<td>51.4 ± 3.6</td>
</tr>
<tr>
<td>12.00 h</td>
<td>41.7 ± 14.5</td>
<td>7.4 ± 0.6</td>
<td>36.3 ± 4.6*</td>
</tr>
<tr>
<td>16.00 h</td>
<td>21.8 ± 5.9</td>
<td>12.5 ± 3.6</td>
<td>36.1 ± 4.8*</td>
</tr>
<tr>
<td>20.00 h</td>
<td>24.7 ± 4.0</td>
<td>6.0 ± 1.0</td>
<td>40.6 ± 3.3</td>
</tr>
<tr>
<td><strong>Day 21</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>8.00 h</td>
<td>12.6 ± 2.2*</td>
<td>53.1 ± 8.8*</td>
<td>25.3 ± 4.1*</td>
</tr>
<tr>
<td>12.00 h</td>
<td>16.4 ± 4.4*</td>
<td>28.7 ± 7.2*</td>
<td>13.7 ± 3.1*</td>
</tr>
<tr>
<td>16.00 h</td>
<td>8.3 ± 2.2*</td>
<td>25.3 ± 11.4*</td>
<td>8.8 ± 2.1*</td>
</tr>
<tr>
<td>20.00 h</td>
<td>6.0 ± 1.6*</td>
<td>23.6 ± 5.2*</td>
<td>12.8 ± 1.8*</td>
</tr>
<tr>
<td><strong>Day 22</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.00 h</td>
<td>11.6 ± 2.5*</td>
<td>34.4 ± 8.4*</td>
<td>8.6 ± 0.6*</td>
</tr>
<tr>
<td>12.00 h</td>
<td></td>
<td>Abortion</td>
<td>Abortion</td>
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<tr>
<td>16.00 h</td>
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<td>Abortion</td>
<td>Abortion</td>
</tr>
<tr>
<td>20.00 h</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Results are the means ± SEM of 8–15 determinations at each time point.  
*P < 0.05 compared with controls; **P < 0.05 compared with values on day 21.  
ND: not determined.

**Serum GH concentrations during pregnancy**

In the present study we have not attempted to study the ultradian rhythm that has been repeatedly described for GH secretion (Saunders et al., 1976; Klindt et al., 1981). Average values obtained in different rats sampled at the same hour are given and represent mean secretion of GH. Serum GH concentrations remained below 20 ng ml⁻¹ during days 4–6 and 11–13 of pregnancy, except on the morning of day 5 (08.00 h) when values increased significantly to 60 ng ml⁻¹ (Fig. 1). Values were low on day 18, but from day 19 onwards, serum GH concentrations increased progressively, reaching concentrations as high as 53 ng ml⁻¹ at 08.00 h on day 21 with a new peak at 12.00 h on day 22, followed by a marked decrease during the afternoon, to a minimum of 10 ng ml⁻¹ at midnight of day 22, which was coincident with an increase in serum prolactin concentrations and a fall in progesterone (see Table 1).
Effect of ovariectomy on serum concentrations of GH, prolactin and progesterone

Ovariectomy performed on day 19 changed the rhythm of serum GH secretion, decreasing the values with respect to controls at 20.00 h on day 19, throughout day 20 and up to 08.00 h on day 21 of pregnancy. There was an acute increase at 12.00 h on day 21 to values similar to those of control rats; thereafter values remained high and not significantly different from control values (Table 1).

Serum prolactin concentrations measured at different times on days 19–22 in intact pregnant rats remained below 10 ng ml\(^{-1}\) until the morning of day 22, and increased significantly thereafter. Serum progesterone concentrations remained between 40 and 70 ng ml\(^{-1}\) until the morning of day 22, and then declined progressively throughout the rest of day 22. Ovariectomy produced an acute fall in serum progesterone concentrations, followed as expected (Vermouth and Deis, 1974) by significant increases in serum prolactin concentrations 8 h after surgery; prolactin concentrations remained high until 20.00 h on day 20. Ovariectomy also blocked the increase in serum prolactin observed on the afternoon of day 22 in control rats.

The increases in prolactin secretion produced by the fall in serum progesterone concentrations were accompanied by significant decreases in serum GH concentrations with respect to intact pregnant rats and, conversely, serum GH concentrations increased after serum prolactin had returned to basal (less than 7.5 ng ml\(^{-1}\)) concentrations.

Effect of mifepristone administration

Mifepristone administration induced a slight increase in serum GH concentration at 16.00 h on day 19 but did not modify them with respect to control rats at the other times measured until 20.00 h on day 20; serum concentrations of GH were significantly lower on days 21 and 22. These rats gave birth by 08.00 h on day 22. Serum progesterone concentrations started to decline in the mifepristone-treated rats by 12.00 h on day 20, reaching basal values 24 h later, whereas prolactin concentrations were low on day 19, but increased by 08.00 h on day 21 and remained high until 20.00 h on day 21 (Table 1). In this group of rats, serum GH concentrations were again significantly reduced with respect to control rats coincident with the increase in serum prolactin.

Effect of tamoxifen

The group of rats that had been given tamoxifen on days 3 and 4 of gestation showed a mean serum GH concentration of 15 ± 4 ng ml\(^{-1}\) (n = 9) after decapitation at 08.00 h on day 5, which was significantly lower (P < 0.001, Student’s t test) than the values observed at the same time in the intact pregnant rats (Fig. 1).

Daily administration of tamoxifen starting on day 17 significantly reduced serum GH concentration, except for peaks at 08.00 h and 16.00 h on day 22 (Table 1). Serum prolactin concentrations in tamoxifen-treated rats were low at all times studied and the increase seen in controls on day 21 was also blocked (Table 1). Serum progesterone concentrations were lower than those of controls at most of the times sampled, and reached values similar to those of controls on the afternoon of day 22, and on the afternoon of day 21. None of the rats had given birth by 20.00 h on day 22, but examination of the uterine content after decapitation on day 22 showed only dead and partially digested fetuses.

Discussion

Any study of GH concentrations in the blood should involve stress-free methods of obtaining samples since handling rats may cause a fall in the release of GH (Takahashi et al., 1971; Terry et al., 1976; Armario et al., 1984) and concentrations are extremely sensitive to anaesthesia. Thus, a brief 2 min exposure to ether has been reported to cause a significant fall in GH concentration (Schalch and Reichlin, 1966; Krulich et al., 1974; Briski et al., 1984). It is also known that major surgical procedures cause a reduction in GH release for two days (Obonsawin et al., 1985) and even 4 days (Eden, 1978) after the operation. However, most previous studies have been performed on male or nonpregnant female rats, and female rats seem to be less sensitive to stress in terms of GH release, particularly when they are pregnant (Schalch and Reichlin, 1966). An interesting finding of the present work is that pregnant female rats seem to have a shorter response to stress in terms of GH release than has been reported for male rats, since after ether-laparotomy, serum GH concentrations were significantly reduced for only 10 min, whereas in male rats the duration of GH depression is longer (Eden, 1978; Obonsawin et al., 1985). This may reflect a general insensitivity of pregnant rats to stress, since prolactin secretion was unaffected by ether-laparotomy, a procedure that readily increases secretion of this hormone in virgin animals (Boehm et al., 1982). These results exclude the possibility that the modifications in hormone concentrations observed in our study were due to stress effects resulting from the methodology used.

Our results showed that a marked increase in serum GH concentrations occurred during the last 4 days of pregnancy, confirming and extending previous studies which were performed by serial sampling of individual rats on selected days of pregnancy (Saunders et al., 1976; Klindt et al., 1981; Carlsson et al., 1990). This increase may be important in the final differentiation of the mammary gland before the initiation of milk secretion and may be related to the marked increase observed in prolactin and GH receptors in the liver observed in the last days of pregnancy (Husman et al., 1985; Jahn et al., 1991).

Regulation of GH release seems to be different to that of prolactin at the end of gestation. The increase observed on the last days of pregnancy could be a consequence of increased oestrogen secretion seen in rats from day 19 (Shaikh, 1971), as oestrogens have been shown to stimulate GH production by the pituitary (Simard et al., 1986; Armario et al., 1984). The high serum GH concentrations found on the morning of day 5 of pregnancy may also be a product of stimulation by oestrogens secreted on this day (Shaikh, 1971), that are necessary for implantation, since the high GH concentrations were inhibited by prior administration of tamoxifen. Furthermore, tamoxifen...
administration in the last days of pregnancy produced significant decreases in serum GH and prolactin concentrations.

The changes in prolactin secretion followed the previously described increases observed after the progesterone fall induced by ovarioectomy (Vermouth and Deis, 1974). Milfeitrostin administration did not induce an immediate increase in prolactin secretion (Deis et al., 1989), but prolactin concentrations rose after 48 h as a consequence of the delayed fall in serum progesterone concentrations. Our results also indicate a role for oestrogens in the increase in prolactin secretion on day 22 (when serum progesterone concentrations are low; Bussmann and Deis, 1979; Nicholas and Hartmann, 1981), as ovarioectomy, as well as tamoxifen administration, completely abolished this rise.

A potential stimulatory action for oestrogens and progesterone on the maintenance of luteal progesterone production in late pregnancy is indicated since both anti-hormones advanced the fall in serum progesterone. A role for both steroid hormones in the maintenance of luteal function in rats has already been described in early and mid-pregnancy (Gibori and Keyes, 1978, 1980; Rothchild, 1980: Kawano et al., 1988; Singh et al., 1988), and our results extend this role to the end of pregnancy.

There appears to be an inverse relationship between prolactin and GH secretion on the last days of pregnancy. In intact, pregnant rats the increase in GH secretion occurred 3 days before the release of prolactin, and when prolactin secretion increased, serum GH concentrations had already fallen. The increases in prolactin secretion observed after ovarioectomy or mifepristone treatment were accompanied by decreases in serum GH, which returned to control concentrations when prolactin concentrations diminished. The reciprocal relationship between prolactin and GH was observed independent of experimental procedure or progesterone concentrations, except for the tamoxifen-treated rats, in which both hormones were depressed, indicating a stimulatory action of oestrogens for both hormones. The stimulatory action of oestrogens on GH release may be evident only in the presence of low concentrations of prolactin. In contrast, any action of progesterone seems to be mediated through its regulation of prolactin secretion.

It is known that many factors regulate GH secretion, but according to our results progesterone does not directly regulate GH release and oestrogen may not be the main factor involved. The inverse relationship between GH and prolactin secretion means that both hormones cannot be released simultaneously. The inhibitory effect of hyperprolactinaemia on GH secretion in female (Esquifino et al., 1987a) and male rats (Esquifino et al., 1987b) and in women (Andersen and Tabor, 1982; Ho et al., 1985) has been reported already.

This work was supported by a grant (PID 9036/01) from the Consejo Nacional de Investigaciones Científicas y Tecnicas (CONICET), Argentina. The authors are indebted to F. E. Guinazu de Di Nasso for her excellent technical assistance. We thank A. F. Parlow and the NIADDK for the rat GH and prolactin kits.

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