EFFECT OF PROSTAGLANDIN $F_{2\alpha}$ ON SERUM PROLACTIN AND LH CONCENTRATIONS IN MALE AND FEMALE RATS

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(Received 10th March 1975)

Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) has been shown to induce prolactin release in pregnant rats (Deis, 1971; Vermouth & Deis, 1972). Treatment with $PGF_{2\alpha}$ may induce lactogenesis in women after early termination of pregnancy (Smith *et al.*, 1972), accompanied by a significant increase in serum prolactin level (Yue *et al.*, 1974). Harms *et al.* (1973) injected PGE_1 into the third ventricle in castrated female rats and found increased plasma prolactin levels, although PGE_2 , $PGF_{1\alpha}$ and $PGF_{2\alpha}$ had no effect. Intraventricular or intravenous injection of PGE_2 induced a significant rise of plasma LH. According to Batta *et al.* (1974), intracarotid injection of $PGF_{2\alpha}$ resulted in a greater release of FSH than LH in ovariectomized rats treated with oestrogen, but had no effect on male rats. In ovariectomized rats primed with oestrogen and progesterone, PGE_1 , PGE_2 and $PGF_{2\alpha}$ caused increases in serum prolactin concentration (Sato *et al.*, 1974a).

Since in a previous study we postulated that the release of prolactin in pregnant rats after administration of $PGF_{2\alpha}$ was probably induced by a rapid decrease of plasma progesterone concentration (Vermouth & Deis, 1972), the present investigation was undertaken in order to establish the effect of $PGF_{2\alpha}$ on prolactin and LH levels in normal male and female rats and in ovariectomized animals treated with oestrogen. Preliminary results have been reported (Vermouth & Deis, 1974).

Virgin male and female rats weighing between 200 and 250 g were used. The occurrence of regular 4-day oestrous cycles was established for intact females by examination of vaginal smears, and the LH and prolactin levels were determined at known stages of the oestrous cycle. Females were ovariectomized 1 to 2 months before use and the effects of $PGF_{2\alpha}$ were tested before oestrogen treatment was initiated. Oestradiol benzoate (1 or 10 μ g) was injected subcutaneously 24 hr before administration of $PGF_{2\alpha}$. The tromethamine salt of $PGF_{2\alpha}$ (Upjohn Co., Kalamazoo) was used and was injected into the jugular vein at 17.00 hours at dose levels of 1, 2.5, 5, 10 or 50 μ g/100 g body weight. Control rats were injected with normal saline. As in a previous study (Deis & Alonso, 1973), 4 mg sodium pentobarbitone (Nembutal: Abbott Laboratories)/100 g body weight were given intraperitoneally at 13.00 hours to all animals to

TEXT-FIG. 1. Effect of different doses of PGF_{2α} on serum prolactin concentration in normal female rats. Each column and the vertical bar represent the Mean $\pm$ S.E.M. Figures above each column show the number of rats used in each group. Hatched columns indicate values in control animals. **** $P < 0.001$; *** $P < 0.005$; ** $P < 0.01$ and * $P < 0.05$.

TEXT-FIG. 2. Effect of PGF_{2α} on serum prolactin concentration in ovariectomized rats before and after treatment with oestradiol benzoate. Each column and the vertical bar represent the Mean $\pm$ S.E.M. and figures above each column show the number of rats used. Hatched column indicates the values in control rats that were ovariectomized but untreated.

Table 1. Concentrations of serum LH (ng/ml) in rats after treatment with PGF_{2α}

Dose of PGF _{2α} (µg/100 g body weight)	Females				Males
	Pro-oestrous	Oestrous	Dioestrous I	Dioestrous II	
0 (control)	118.3 ± 9.6 (6)	109.8 ± 12.7 (6)	102.7 ± 6.3 (12)	124.0 ± 9.9 (5)	111.0 ± 8.3 (6)
1	107.0 ± 6.8 (3)				
2.5	125.6 ± 15.5 (6)	116.0 ± 12.1 (4)	83.2 ± 10.3 (4)	103.8 ± 2.3 (5)	
5	132.9 ± 3.2 (7)			110.0 ± 10.3 (5)	92.4 ± 5.0 (4)
10	140.0 ± 6.9 (5)	142.7 ± 12.8 (5)	113.1 ± 11.2 (8)	101.7 ± 3.3 (7)	85.0 ± 4.6 (5)
50	142.8 ± 4.1 (4)				

Values are Means ± S.E.M.; the numbers of rats are given in parentheses.

prevent any spontaneous release of prolactin or LH. At the time of treatment with PGF_{2α} or normal saline, light ether anaesthesia was induced to allow rapid injection of the substances into the jugular vein, a procedure which took less than 30 sec. Fifteen minutes after the injection (17.15 hours) blood samples were obtained by heart puncture. Serum prolactin and LH concentrations were assayed by the radioimmunoassays of Niswender *et al.* (1969) and Monroe *et al.* (1969), respectively, each at two dose levels. The results are expressed in terms of the NIAMDD-Rat-Prolactin-RP-1 and NIAMDD-Rat-LH-RP-1 standards. All serum samples were measured in a single assay to eliminate between-assay variations. Student's *t* test was used to assess the level of significance.

Prolactin levels in male rats rose from 27.9 ± 2.0 (S.E.) ng/ml in animals given saline to 67.8 ± 7.7 ng/ml ($P < 0.001$) and 49.9 ± 8.7 ng/ml ($P < 0.02$) after treatment with 5 and 10 µg PGF_{2α} respectively.

A significant increase in serum prolactin was found in the pro-oestrous rats in response to all the doses of PGF_{2α} except for the 1 µg dose. Only the 10 µg dose of PGF_{2α} caused a significant increase in rats in oestrus or dioestrus I; no change in prolactin values was found in rats treated during dioestrus II (Text-fig. 1).

The effects of PGF_{2α} on prolactin levels in ovariectomized rats primed with oestrogen are shown in Text-fig. 2. A significant rise in prolactin levels occurred only in ovariectomized rats primed with 10 µg oestradiol benzoate 24 hr before a dose of 10 µg PGF_{2α}.

Serum LH concentrations in males and females were not significantly affected by PGF_{2α} treatment (Table 1).

These results suggest that PGF_{2α} may influence pituitary prolactin release without altering LH secretion. The site of action and physiological role of PGF_{2α} in the regulation of prolactin release are uncertain. It is probable that PGF_{2α} may act at the hypothalamic level, since prostaglandins are present in most parts of the brain, including the hypothalamus (Holmes & Horton, 1968). Furthermore, it has been suggested that prostaglandins may play an important role in modifying or modulating the actions of other transmitters in the brain (Bradley *et al.*, 1969).

The present results, and those of other workers (Chamley & Christie, 1973; Harms *et al.*, 1973; Batta *et al.*, 1974), indicate that PGF_{2α} is not involved in the release of LH. However, Sato *et al.* (1974b) showed that PGF_{2α} augmented LH concentrations in the serum of ovariectomized rats treated with oestrogen and progesterone, but was less effective than PGE₁ and PGE₂. A similar finding has been reported for the hamster (Saksena *et al.*, 1974) and the ewe during the breeding season (Carlson *et al.*, 1973).

Our findings suggest that the effect of PGF_{2α} on prolactin release is oestrogen-dependent. The discrepancy between the present results and some of those reported by other authors may be due to differences in the experimental technique. It is possible that sodium pentobarbitone may facilitate the effect of PGF_{2α} on prolactin release, as has been observed for PGE₁ and PGE₂ on LH release (Spies & Norman, 1973; Tsafiriri *et al.*, 1973). Further studies are required in order to establish whether PGF_{2α} plays a role in the release of prolactin on the afternoon of the day of pro-oestrus.

We thank Dr John E. Pike of Upjohn Co. for the PGF_{2α} and Abbott Argentina for the Nembutal. We are grateful to the National Institute of Arthritis, Metabolic and Digestive Diseases, rat pituitary hormone distribution programme for the radioimmunoassay kit for prolactin and LH. This work was supported by a grant from the Consejo Nacional de Investigaciones Científicas y Técnicas of Argentina of which R.P.D. is a Career Scientist and N.T.V. is a Post-doctoral Fellow.

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