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ESTRONE AND PROGESTERONE PLASMA LEVELS OF NORMAL COWS AND COWS WITH PARTURIENT PARESIS*

By

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EDQVIST, L.-E., L. EKMAN, B. GUSTAFSSON and J.-O. LINDELL: *Estrone and progesterone plasma levels of normal cows and cows with parturient paresis*. Acta vet. scand. 1974, 15, 587—596. — Blood plasma concentrations of estrone and progesterone, calcium and inorganic phosphorus were measured in 22 cows (Swedish Red and White Breed) from 4 weeks prepartum up to 6 days post partum. Ten cows with parturient paresis had Ca levels below 6 mg/100 ml. Data from plasma analyses in individual cows were grouped in the following periods: 28—22, 21—15, 14—8, 7—6, 5—4, 3, 2, 1 day(s) before parturition and 1, 2, 3—6 days after parturition. Statistical comparisons of the levels of the hormones and the ratio progesterone/estrone did not reveal any significant differences between the paretic and normal cows at any time period. The results do not support the theories that high systemic levels of estrogens or an imbalance between estrogen and progesterone predispose towards parturient paresis.

cows; parturient paresis; estrogen; progesterone.

In spite of intensive research many aspects of the etiology and pathogenesis of parturient paresis in the dairy cow are still unknown. As parturition in the cow is a complicated endocrinologic process, the involvement of certain hormones in the pathogenesis of parturient paresis has been suggested. It has been emphasized that the gonadal hormones and the estrogens in particular might have an effect on calcium metabolism and predispose to the disease (*e.g.* Jönsson 1960, Payne *et al.* 1965, Stott 1968).

The effects of estrogens on bone varies from species to species and with age (*Bauer et al.* 1961). A stimulation of bone accretion has been seen in mice (*Ranney* 1959) but not in adult

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rats (McLean & Urist 1955). In mice, estrogens seem to oppose the function of parathormone in promoting bone resorption (Ranney). Stott proposed that a high systematic estrone level in a cow at parturition might oppose the action of parathormone on bone and predispose such a cow for parturient hypocalcemia. This estrogen effect might be counteracted by progesterone which is known to have an anti-estrogenic activity.

Muir et al. (1972) reported that bone calcium resorption was not inhibited by increasing blood estrogen by injection to levels calculated to occur at parturition. However, the injected estrogen caused decreased feed intake and thus reduced the amount of calcium available for absorption from the gastro-intestinal tract. The depressing effect of estrogen on feed intake could be partially overcome by injection of progesterone.

The aim of the present investigation was to compare the peripheral blood plasma levels of estrogen and progesterone during the peripartal period of cows suffering from parturient paresis with the levels of those in corresponding healthy cows. Only limited studies restricted to progesterone have earlier been presented (Edqvist et al. 1970 a).

MATERIAL AND METHODS

Twenty-two cows of the Swedish Red and White Breed (SRB) were examined. Their age varied between 4 and 7.5 years (Table 1). Thirteen of the cows had clinical parturient paresis at their previous calving, i.e. they were parturient paresis prone cows. At the present calving 8 of these cows had parturient paresis, i.e. they became paretic and showed plasma levels of Ca below 8 mg/100 ml (cf. Jönsson 1970, Jonsgård 1972). Parturient paresis appeared also in two cows not considered prone to the disease. Consequently the clinical material comprised 10 cows with parturient paresis and 12 cows without symptoms of paresis and which had plasma Ca levels above 8 mg/100 ml around parturition.

Fourteen of the cows belonged to a research station and were kept there throughout the experimental period. Four cows were kept and examined at a private herd. Four cows were brought to the Royal Veterinary College from different farms at least 4 weeks before expected delivery. The cows were fed hay, ensilage and concentrate.

Table 1. Details on the experimental animals and procedures.

Cow no.	Age (years)	Susceptible (+) or non-susceptible (-) to paresis	Paresis (+) or not (-)	Retained placenta (+) or not (-)	Start of blood sampling before parturition (days)	Number of daily blood samples before parturition	Duration of pregnancy (days)
1	6½	+	+	—	7	4	279
2	7	+	+	—	9	4	280
3	6½	+	+	—	11	6	279
4	7	+	+	—	29	12	283
5	6	+	+	+	16	4	277
6	4	—	+	—	1	1	280
7	5	+	+	—	4	3	278
8	4½	—	+	—	7	5	276
9	6½	+	+	—	22	18	290
10	7	+	+	+	21	19	285

11	4	—	—	—	8	7	281
12	4½	—	—	—	21	13	281
13	6	+	—	—	20	16	278
14	4½	—	—	—	23	9	283
15	5½	—	—	—	31	17	276
16	6	—	—	—	22	9	281
17	4	—	—	+	8	6	279
18	7½	—	—	—	15	13	284
19	7	+	—	—	25	24	279
20	6½	+	—	+	24	18	279
21	7½	+	—	—	15	12	276
22	4½	+	—	—	22	16	285

Blood sampling from the cows in general started 4 to 2 weeks before expected parturition. In a few cases start of blood sampling commenced less than 1 week before calving (Table 1).

Data obtained from blood analysis of individual cows were grouped accordingly: 4 weeks (28—22 days), 3 weeks (21—15 days), 2 weeks (14—8 days), 7—6 days, 5—4 days, 3 days, 2 days, and 1 day before parturition, 1 day, 2 days and 3—6 days after parturition. During the time periods of several days' duration usually more than 1 blood sample was taken from each cow. In such cases the mean values for all measurements of a single parameter during the period have been calculated and used in the statistical treatment of the data.

The following blood plasma analyses were performed: Ca, inorg. P, progesterone and estrone. Plasma Ca was determined by atomic absorption spectroscopy, inorg. P with a Technicon Auto

Analyzer (Technicon, Method File N-4C), progesterone and estrone in plasma according to *Edqvist et al.* (1970 b) and *Edqvist & Johansson* (1972), respectively. Estrone was determined with a rapid radioimmunoassay technique utilizing an antiserum to estradiol-17 β 17-succinyl-bovine serum albumin (*Edqvist & Johansson*). The cross-reaction percentage of this antiserum with estrone was 65 % (cross reaction with estradiol-17 β = 100 %) (*Boilert et al.* 1973).

RESULTS

The gestation period of all cows in the present study (Table 1) was within the normal limit for the breed used, 280.8 ± 5.7 (s) days (*Rendel* 1958). The course of parturition was normal in all cows except no. 7 which became paretic 4 hrs. before parturition. The paresis was combined with uterine inertia and the cow was treated with Ca intravenously. The calf had to be manually extracted. Cow no. 17 delivered twins in a normal parturition. With exception of cow no. 7 the parturient paresis occurred within 24 hrs. of parturition. Conventional treatment with infusions of Ca preparations was given. Eight of the 10 cows with paresis recovered after 1 or 2 infusions. Cows nos. 1 and 5 became downers (*cf. Jönsson & Pehrson* 1969) and were slaughtered within a week of parturition. Two cows in each group developed retained placenta (Table 1).

Plasma Ca or inorg. P concentrations did have a statistically significant difference between cows with paresis and normal cows from the different samples from 4 weeks to second sample preceding parturition (Table 1). The mean values for Ca at each sample period varied between 8.9 and 9.9 mg/100 ml in the paretic cows. Corresponding ranges for inorg. P were 4.1—5.1 mg/100 ml, respectively, during the period 4 weeks to 10 days before parturitions of Ca and inorg. P between 4.0—7.7 mg/100 ml and 1.4—4.2 mg/100 ml, respectively. In normal cows the mean Ca and inorg. P levels were 9.4—10.2 mg/100 ml and 4.6—5.7 mg/100 ml, respectively, during the period 4 weeks to 10 days before parturition. In the normal group the Ca and inorg. P levels dropped to mean values of 8.8 and 4.6 mg/100 ml, respectively, at the last sampling before parturition. Thereafter they remained at about these levels throughout the experimental period (Table 1).

The mean peripheral plasma levels of estrone and progesterone are presented in Fig. 1. Statistical analyses (Student's t-test)

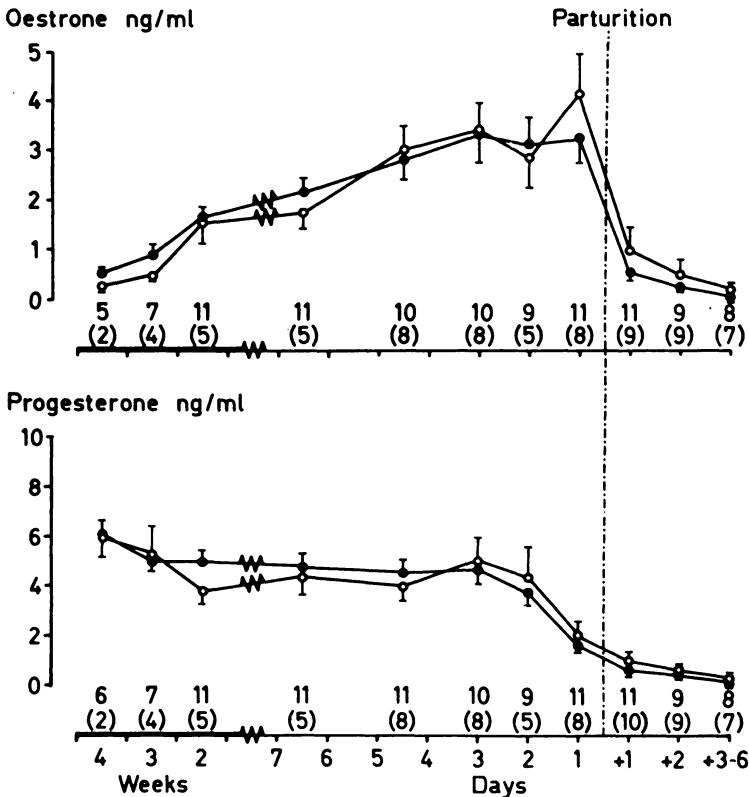


Figure 1. Plasma estrone and progesterone in healthy cows (●—●) and in cows with parturient paresis (○—○). Mean concentrations \pm s.e.m. for the number of cows at each time indicated on the abscissa are given. Figures in brackets denote the number of cows with parturient paresis.

did not reveal any significant differences between the 2 groups of cows at any time interval for either estrone or progesterone. The plasma level of estrone increased gradually from values of about 0.5 ng/ml at 4 weeks before parturition to values of about 3.5 ng/ml at the last sample, usually taken less than 1 day before parturition. After parturition the levels dropped dramatically to values of about 0.7 ng/ml. On days 3—6 after parturition the mean peripheral plasma level of estrone was below 0.25 ng/ml. The mean progesterone values in blood plasma varied between 4 and 5 ng/ml from 4 weeks until the sampling about 2 days before parturition. Thereafter the values dropped and mean values of about 2 ng/ml were recorded from the last sample before delivery.

Table 2. Progesterone/estrone concentration ratio, Ca levels and inorg. P levels before and after parturition. Mean \pm s.e.m. are given; n denotes number of cows.

	Weeks			Days							
	4	3	2	7-6	5-4	3	2	1	+1	+2	+3-6
<i>Progesterone/estrone ratios; Paretic cows</i>											
\bar{x}	21.96	12.59	5.00	2.96	1.71	1.71	1.63	0.60	2.39	2.22	3.0
s.e.m.	8.95	3.80	3.07	0.93	0.46	0.40	0.49	0.15	0.76	0.41	1.4
n	2	4	5	5	8	8	5	8	9	9	7
<i>Non paretic cows</i>											
\bar{x}	14.87	7.28	3.66	2.47	1.86	1.77	1.57	0.53	1.81	2.92	3.8
s.e.m.	3.56	1.48	0.55	0.33	0.25	0.39	0.38	0.09	0.43	0.78	0.9
n	5	7	11	11	10	10	9	11	11	9	8
<i>Ca levels mg/100 ml; Paretic cows</i>											
\bar{x}	9.4	9.0	8.9	9.1	9.6	9.9	9.0	8.2	7.2	6.4	—
s.e.m.	0.30	0.40	0.31	0.45	0.32	0.53	0.47	0.62	0.81	0.68	—
n	2	3	4	4	6	6	4	5	6	4	—
<i>Non paretic cows</i>											
\bar{x}	9.6	9.4	9.6	9.7	10.2	10.2	10.0	8.8	8.6	8.6	8.7
s.e.m.	0.12	0.42	0.16	0.19	0.15	0.28	0.28	0.38	0.47	0.24	0.2
n	6	6	9	9	8	9	8	9	9	8	7
<i>Inorg. phosphorus levels mg/100 ml; Paretic cows</i>											
\bar{x}	4.5	5.1	4.9	4.7	5.0	5.0	4.7	4.1	2.6	4.3	—
s.e.m.	0.75	0.43	0.33	0.33	0.31	0.45	0.25	0.48	0.38	0.94	—
n	2	3	4	4	6	6	4	5	6	5	—
<i>Non paretic cows</i>											
\bar{x}	5.7	5.0	5.3	5.3	5.2	5.3	5.5	4.6	4.5	4.7	4.7
s.e.m.	0.29	0.48	0.21	0.20	0.28	0.29	0.25	0.38	0.46	0.39	0.3
n	5	6	9	9	8	9	8	9	9	8	7

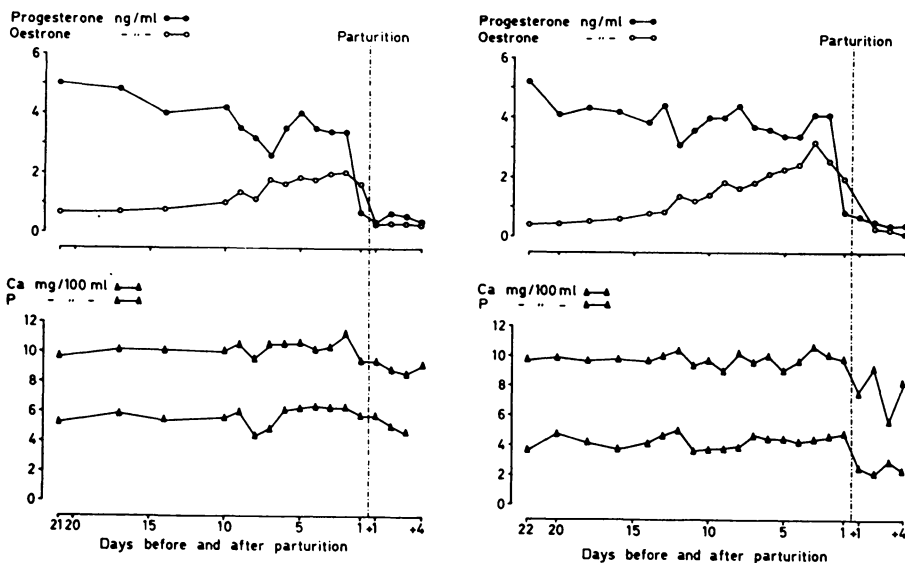


Figure 2. Plasma estrone, progesterone, calcium and inorg. phosphorus in a normal non-susceptible cow (no. 12) (left) and in a cow (no. 9) (right) with parturient paresis immediately after delivery.

After parturition the progesterone levels decreased further to values below 0.5 ng/ml at the last sample. The progesterone/estrone concentration ratio for the various time intervals studied can be seen in Table 2. At no time interval was there any statistically significant difference between the ratios from the 2 groups of cows.

Plasma concentrations of Ca, inorg. P, estrone and progesterone in a typical healthy cow, not prone to paresis (no. 12), are illustrated in Fig. 2. The corresponding values for a parturient paresis prone cow which became paretic are presented in the same figure.

DISCUSSION

The clinical course of parturient paresis in the 10 cows was typical for the classical form of the disease. The same is true for the blood plasma patterns of Ca and inorg. P concentrations. The routine treatment of the cows with intravenous infusions of commercial calcium preparations had also good therapeutic effects in all cows except 2 which became downers.

The plasma levels and patterns of estrogen and progesterone in the paretic cows, as well as the normal cows, were very similar to the previously reported normal values (Edqvist et al. 1972, Henricks et al. 1972, Smith et al. 1973). In a statistical comparison of the levels of the hormones and the concentration ratio progesterone/estrone at various time intervals before and after parturition in paretic and normal cows, no statistically significant differences were found at any time.

The criterion for grouping the cows in this study was presence of parturient paresis. A statistical comparison has, however, also been made between susceptible and non-susceptible cows without considering the actual occurrence of parturient paresis. With this grouping there were also no significant differences between the groups for any of the hormonal parameters examined.

The results of this study do not lend any support to the theories put forward by several researchers (Payne et al. 1965, Stott 1968, Kronfeld 1971): viz. that higher than normal systemic levels of estrogens or an imbalance between estrogens and progesterone are involved in the pathogenesis of parturient paresis. It should be pointed out, however, that in this investigation it was not possible to individually control the intake of various food constituents. This means that there might have been minor differences in the intake of Ca and P which might have had an effect on the results obtained. A continuing study is examining the gonadal hormone in blood plasma of cows with individually controlled feed intake.

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SAMMANFATTNING

Plasmanivåer av östron och progesteron hos normala kor och hos kor med puerperal pares.

Koncentrationerna av östron, progesteron, Ca och oorg. P i blodplasma bestämdes på 22 SRB-kor från fyra veckor före partus till sex dagar efter partus. Tio av korna fick puerperal pares med plasma-Ca under 6 mg/100 ml. Resultaten av plasmaanalyserna från enskilda kor sammanfördes inom följande tidsperioder: 28—22, 21—15, 14—8, 7—6, 5—4, 3, 2, 1 dagar före partus och 1, 2, 3—6 dagar efter partus. Statistiska jämförelser av hormonnivåer liksom av kvoterna progesteron/östrogen visade inga signifikanta avvikelser vid någon period. Undersökningens resultat stöder ej teorierna om en hög östrogennivå eller en inbalans mellan östrogen och progesteron som predisponerande för puerperal pares hos nötkreatur.

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