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ENDOCRINOLOGY OF PARTURITION IN THE PIG

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ABSTRACT

Endocrine and physiological events that precede and accompany parturition in the sow occur in a sequential fashion starting with a slow increase in estrogens from about three weeks prior to parturition. The luteotrophic role of LH visible as a distinct LH-progesterone relation is present at three weeks prior to parturition but can no longer be seen at one to two days prior to expulsion. Progesterone has not completed its decline during expulsion. A rather sharp and transient increase in plasma relaxin is known at about one day prior to expulsion. Corticosteroids are elevated also during the last 24 hours before parturition with a peak during expulsion. Oxytocin levels remain at baseline levels till progesterone has reached values below 10 ng/ml when a two step sharp increase in plasma oxytocin can be observed; one step prior to expulsion and a second during expulsion. Concomitant to endocrine changes the uterine EMG displays characteristic patterns, but is insensitive to oxytocin four days prior to parturition.

INTRODUCTION

Prepartal sequences of individual physiological events have been established in most domestic species. The pig differs from other species in several aspects: it is intolerant to ovariectomy right to the very end of pregnancy which implies that extraovarian progesterone is not sufficient to maintain pregnancy (Kimura and Cornwell, 1938; Short, 1956; Rombauts et al., 1965; Parvizi et al., 1976). Only excessively high levels of exogenous corticosteroids will induce parturition (First and Staigmiller, 1972; Bosc, 1974), and the pig is polytoccous. Although data on endocrine and physiological changes in the peripartal pig are available, it has not yet been attempted to integrate these into a coherent presentation. We shall attempt to draw a picture on endocrine and physiological events preceeding and accompanying parturition in the sow. Some details of a joint effort have been reported on this symposium by Forsling et al., Taverne et al. and Macdonald. The pig has also been incorporated into a review by Thorburn et al., 1977.

Late gestation

The pituitary of the pig must be present to maintain pregnancy. Hypophysectomy between day 4 and 70 (du Mesnil du Buisson et al., 1964; du Mesnil du Buisson and de Namurs, 1969) causes abortion, while pituitary stalk section on day 70 or 90 obviously maintained pregnancy for further 20 days (du Mesnil du Buisson and de Namurs, 1969). Hypophysectomy on day 70, 80 or 90 (Kraeling and Davis, 1974) also resulted in abortion within 60 hrs after hypophysectomy. Since pregnancy was continued when progesterone was given after hypophysectomy (du Mesnil du Buisson and de Namurs, 1969) and since pycnotic corpora lutea were present in hypophysectomized sows (Kraeling and Davis, 1974), it was natural to conclude that a pituitary luteotrophic factor is necessary to maintain normal corpus luteum function in pregnancy. The hypophyseal luteotrophic factor had been suggested long ago to be LH (Brinkley et al., 1964; Anderson et al., 1967; Cook et al., 1967). It was not until recently that our group (Parvizi et al., 1976) found a very peculiar relationship between prepartal circulating LH and progesterone levels (Fig. 1). Three weeks prior to parturition each episodic LH peak was followed by an episodic progesterone peak. 41 to 17 hrs before parturition, however, progesterone values fluctuated erratically on a lower level and were independent of the still present LH episodes. This effect is likely to start

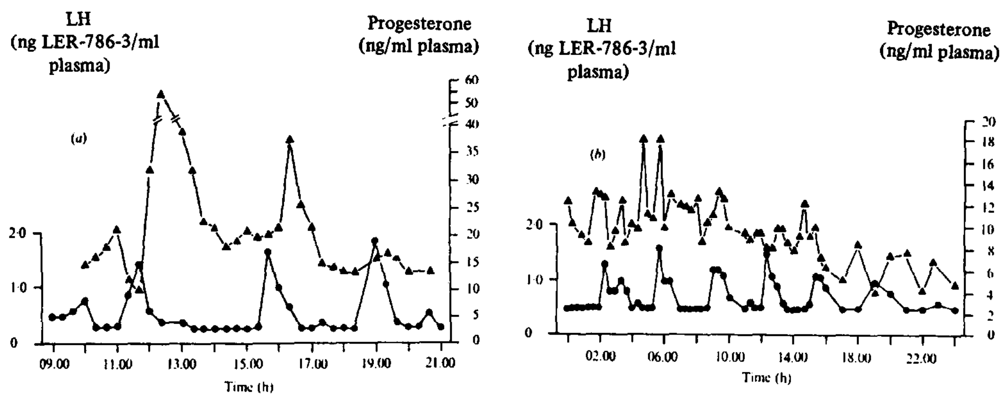

Fig. 1. Plasma LH (▲) and progesterone (●) during (a) a 12 h period 3 weeks, and (b) a 24 h period 41-17 h, before parturition in a miniature sow. Note that in (a) each increase in LH is followed by an increase in progesterone but in (b) this relationship is greatly diminished. (From Parvizi et al., 1976).

earlier than 48 hrs prior to parturition, since there is general agreement, that progesterone has commenced its decline by then (Killian et al., 1973; Molokwu and Wagner, 1973; Robertson and King, 1974; Baldwin and Stabenfeldt, 1975; Parvizi et al., 1976). There are several factors that could make the corpus luteum less sensitive to the luteotrophic action of LH two days prior to parturition. An increase in prostaglandin levels could be possible: no prepartal plasma prostaglandin levels are however yet available prior to parturition from the pig. Parturition is readily induced by prostaglandins with a concomitant decrease in plasma progesterone (Bosc et al., 1975; Gustavsson et al., 1976; Wetteman et al., 1977). Another ovarian hormone of potential importance for processes leading to parturition is relaxin (Hisaw and Zarrow, 1948; Belt et al., 1971). It has been suggested to be of non-corpus luteum (Albert et al., 1947) as well as of corpus luteum origin (Belt et al., 1971). Recent fluorescent antibody studies found relaxin to be confined to the corpus luteum only (Larkin et al., 1977). Unlike progesterone it keeps a rather low profile during pregnancy (Fig. 2) starting to appear around 28 days of pregnancy. Only near term does relaxin reach maximal values to disappear again shortly prior to expulsion of the fetus (Anderson et al., 1973; Sherwood et al., 1975). Relaxin secretion is readily increased by prostaglandins (Sherwood et al., 1976). In bioassays porcine relaxin enlarges the interpubic ligament of estrogen-primed mice, which may also be one function during parturition in the sow. Relaxin also inhibits uterine activity (Porter and Lincoln, this symposium) and may thus serve as a regulatory mechanism safeguarding the uterus from contractions until expulsion is due.

From other species it is known that estrogens elevate prostaglandin levels prior to parturition (Challis et al., 1972; Liggins, 1973). Unlike the sheep, where estrogen does not increase until approx. 24 hrs prior to expulsion of the fetus, a slow but steady increase in plasma estrogen commences already 3 weeks prior to parturition in the pig (Robertson and King, 1974) (Fig. 2). Since ovariectomy does not abolish the increase in estrogens (Fèvre et al., 1968), the surge must be of other possibly placental origin. It can be assumed that the sequence of early mechanisms of events are elevations of estrogens, prostaglandins, decrease in luteolytic sensitivity, increase in relaxin, progesterone decline. Unknown is the exact source and function of the parallel increase in estrone sulphate at late stages of gestation, although it has been found in the uterine vein and allantoic fluid (Robertson and King, 1974).

No particular changes in plasma corticosteroids are noticeable during late gestation until 1 - 2 days prior to parturition (Killian et al., 1973; Molokwu and Wagner, 1973; Fèvre, 1974; Baldwin and Stabenfeldt, 1975). Obviously there is no decisive role corticosteroids play at this early stage. This suggestion is supported by the failure to induce parturition during late pregnancy with other than excessive doses of corticosteroids (Boscu et al., 1974).

Plasma oxytocin levels remain several days - prior to parturition still close to their lower level of detection (Forsling et al., 1979). The uterine EMG recorded during late gestation showed a low frequency, low amplitude pattern(Fig. 5).

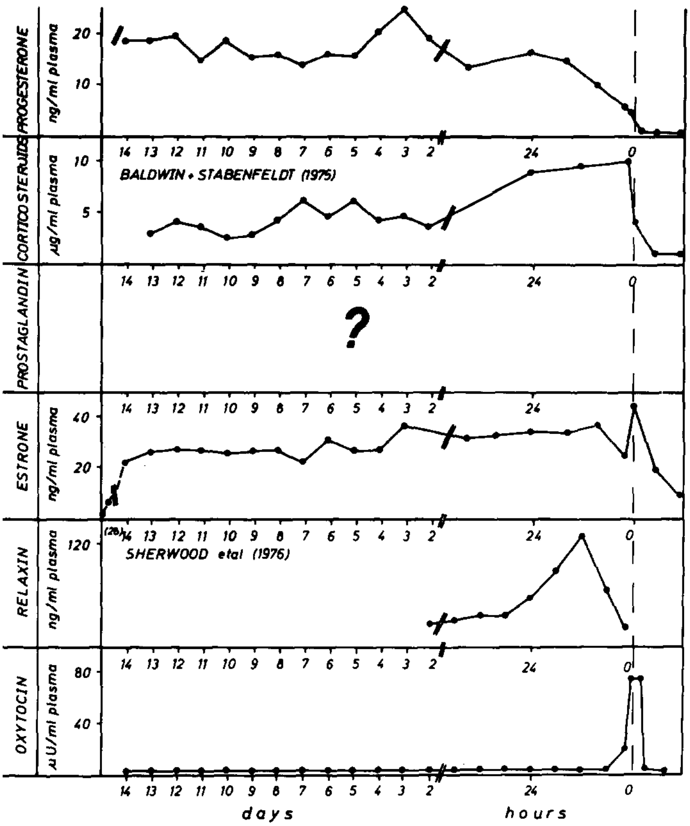

Fig. 2. Summary of endocrine events prior and during parturition in the sow. Where no reference is made, curves are based on own data.

Expulsion

During the last 48 hrs prior to parturition and during expulsion of the fetus dramatic changes can be observed in the endocrine system, affecting progesterone, estrogen, corticosteroids, oxytocin, the uterine EMG and behaviour. Since many changes fall so close together, it is not always possible to establish an exact sequence of events, which was rather easy to do during the "slow motion phase" prior to the final stages. The first event that had already been mentioned is the fast rise - fast fall of relaxin. Soon after, plasma corticosteroids rise to peak levels under the expulsion of the offspring (Fig. 2). They fall again to prepartal levels immediately with the termination of delivery. It has been suggested from other species (Challis et al., 1977) that synacthen (Beta 1-24 ACTH)-infusion increases maternal estrogen in the sheep. It may be this mechanism which leads to the final surge of estrogen immediately prior and under expulsion of the fetuses. Progesterone - though declining continuously - does not reach baseline values until under expulsion and after. A first elevation in oxytocin

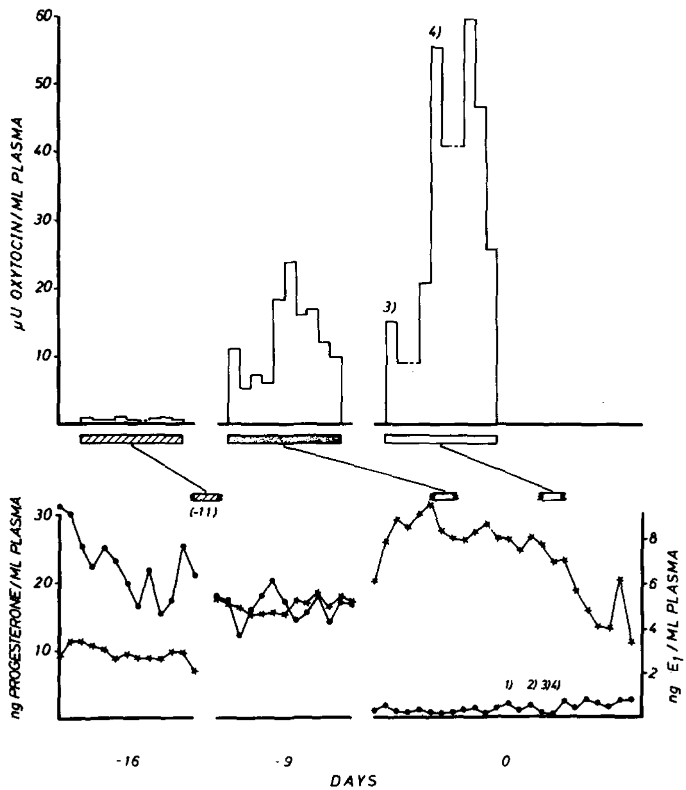

Fig. 3. Plasma oxytocin (upper graph), progesterone (•) and estrone (✶ E_1) concentrations between day -16 and during parturition in a miniature sow. The oxytocin time scale is exploded over the time indicated at the lower graph. Each vertical bar represents a 2 min sampling period. Steroid data on day -16 were taken at 10 min intervals for 2 hrs. At 1) the first piglet is born, at 2) the second, at 3) the third and fourth and at 4) the fifth. Oxytocin is elevated immediately prior to the first expulsion and reaches extreme levels during and after the expulsion of the fifth, but not of the third and fourth piglet. Plasma progesterone is very low, when oxytocin levels are elevated.

values is seen only a few hours prior to expulsion and depends on the fall in progesterone which had to be below 10 ng/ml (Fig. 3). We may assume that other hormonal changes set the stage for oxytocin to be released. We know that prostaglandins cause the release of oxytocin immediately after parturition in the pig (Fig. 4), and it is known that the synthetic estrogen causes the release of oxytocin (Roberts and Share, 1969). Prostaglandins are very likely to be present prior to oxytocin release when plasma estrogens have reached high preexpulsion levels. Therefore we must assume that progesterone is the final blocking element that has to be below a certain threshold to allow oxytocin to be released and expulsion to take place (Forsling et al., 1979). On the other hand parturition is prolonged when progesterone has been given to sows

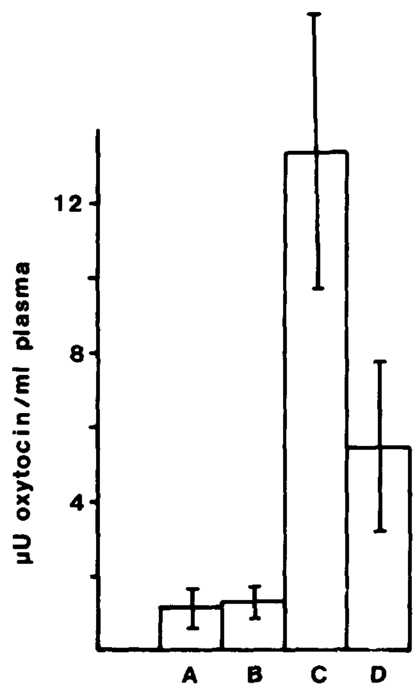

Fig. 4. Prostaglandin induced secretion of oxytocin in four miniature sows six days post partum. A = 0-60 min; at 60 min 1 ml solvent was given. B = 65-120 min; at 120 min 5 mg $PGF_{2\alpha}$ (Prostavet) was given. C = 125-180 min. D = 185-240 min. Samples were taken at 10 min intervals, but at 5 min intervals from 0-20 min, 60-80 min and 120-140 min (Data from Ellendorff et al., 1979).

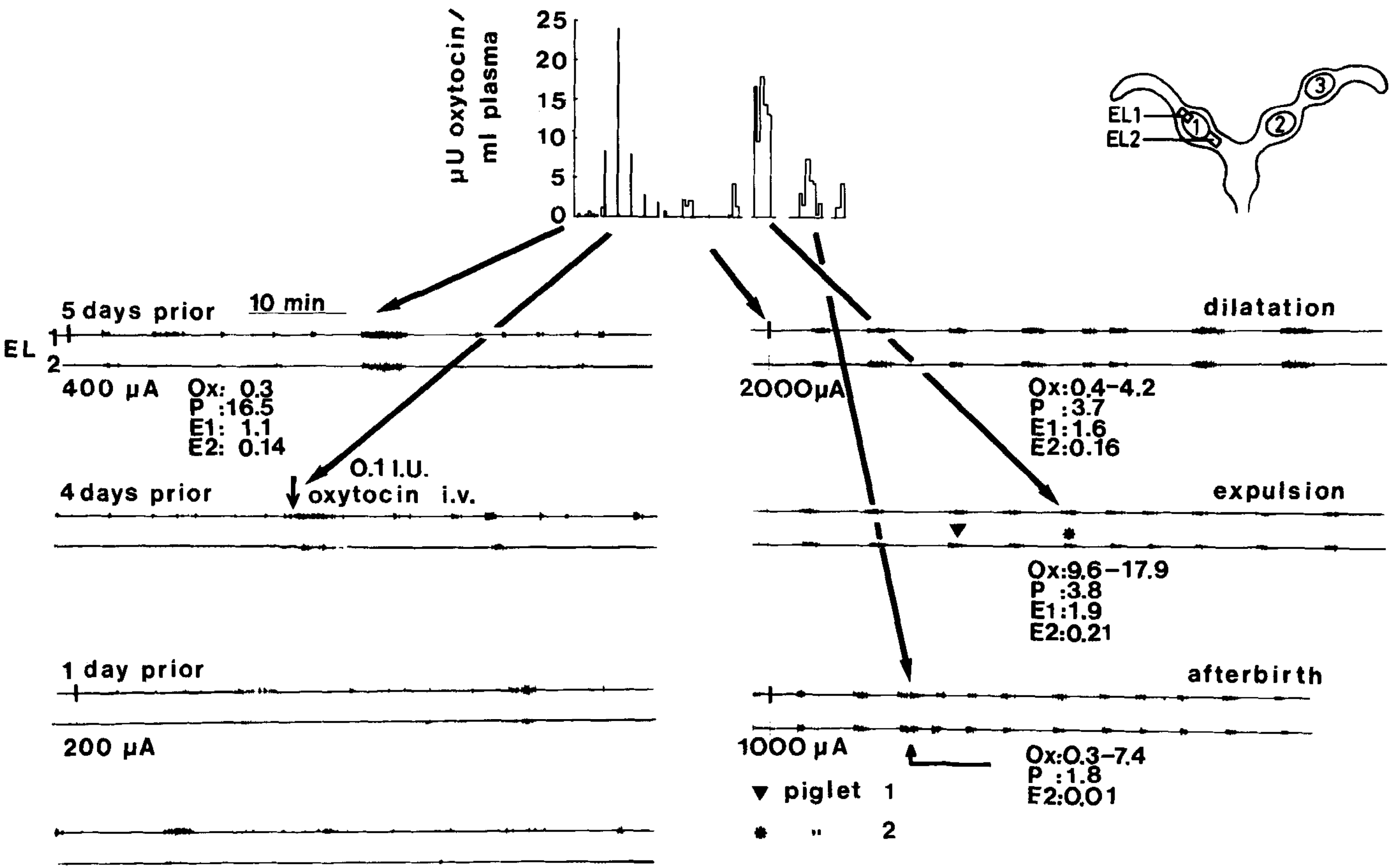

Fig. 5. Integrated presentation of endocrine and myometrial activity prior and during parturition, Details of electromyography are described in Taverne et al. (this symposium). Ox = oxytocin; P = progesterone; E_1 = estrone; E_2 = estradiol; El1, El2 = electrode 1 and 2.

immediately prior to the onset of parturition (Minar and Schilling, 1970). Another phenomenon is a tremendous rise of oxytocin under the expulsion of the fetuses.

This is possibly a reflex release due to mechanical stimulation of the birth channel. We know that the fetus is not only passively pushed through the birth channel, but actively participates in the process, from two observations: first, turning of the fetus prior to expulsion is frequent (Taverne et al., 1977). Secondly, unpublished X-ray cinematographic studies of the process of parturition in the miniature sow have shown that fetuses are active to the degree of "running" through the birth channel.

Concurrent recordings of uterine EMG and relation to circulating hormone levels yielded some interesting aspects (Fig. 5).

First, uterine EMG patterns are clearly different prior to parturition, during expulsion of the fetus and during the expulsion of the afterbirth (Taverne et al., this symposium). Second, five days prepartum EMG-patterns are associated with low oxytocin in the presence of still elevated progesterone titers and estrogen values that are on an increasing slope. During the dilatatory stage of parturition progesterone has declined considerably, allowing plasma oxytocin to increase. Estrogens have further increased their plasma concentrations. The expulsion of the second fetus is characterized by a dramatic increase in plasma oxytocin levels and a further rise in plasma estrogens. Only after termination of fetal expulsion has progesterone reached its lowest levels and estradiol has already declined dramatically. Suckling induced a rise in oxytocin, the EMG-pattern has assumed a high frequent, short duration pattern. Third, oxytocin injection resulting in levels comparable to expulsatory values is not able to alter uterine EMG patterns for any extended period of time.

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