PRO-OESTROUS SURGE IN PLASMA PROGESTERONE IN THE COW

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A preovulatory rise in peripheral plasma progesterone concentration has been reported in women, monkeys, rats, mice, hamsters, guinea-pigs and rabbits (Kazama & Hansel, 1970). In the cow, a preovulatory rise in plasma progesterone levels was not found when blood samples were collected once daily (Shemesh, Lindner & Ayalon, 1971) every 2 to 3 hr for 10 to 12 hr, starting with the onset of oestrus (Henricks, Dickey & Niswender, 1970), or every 6 hr from the onset of oestrus until ovulation (Kazama & Hansel, 1970). The latter authors noted the possibility that a transient rise and fall in plasma progesterone concentration may have been missed due to infrequency of sampling during the pro-oestrous period. The present investigation was undertaken to examine this possibility.

The blood samples examined were aliquots from the same collections of jugular vein blood from nine lactating Friesian cows, which were used for determining oestradiol levels in peripheral blood during the oestrous cycle (Shemesh, Ayalon & Lindner, 1972). Checks for oestrous behaviour were made twice daily, using a bull with a surgically deflected penis; acceptance of mounting was taken as evidence of behavioural oestrus. Starting 24 hr before the expected onset of oestrus, blood collections and tests for oestrus were carried out every 4 hr until the time of ovulation, which was determined by rectal palpation every 4 hr, starting 8 hr after the onset of oestrus. In this study, the blood samples examined were those collected every 4 hr, from 24 hr before until 24 hr after the onset of oestrus. Plasma progesterone was determined using the competitive protein-binding (CPB) assay (Shemesh *et al.*, 1971).

The results found for plasma progesterone concentrations during this 48-hr period are presented in Text-fig. 1. In addition to plasma progesterone concentrations for this period, Text-fig. 2 includes the plasma oestradiol values found for these cows, using the CPB assay (Shemesh *et al.*, 1972).

The results for the period studied show a peak in plasma progesterone concentration (2.28 ± 0.32 ng/ml) occurring about 16 hr before the onset of oestrus. This surge was of short duration, and progesterone values 4 hr later had already declined to the low levels found before the brief rise in concentration. Low levels of progesterone were evident for the rest of the intervals examined. A pre-ovulatory progesterone peak occurring after the onset of oestrus was not apparent, which is in accord with the findings of Kazama & Hansel (1970)

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TEXT-FIG. 1. Peripheral plasma progesterone levels in nine cows around the time of oestrus. Vertical bars indicate $\pm$ S.E.

TEXT-FIG. 2. Comparison between plasma levels of progesterone (---) and oestradiol-17 β (—) in nine dairy cows around oestrus. Vertical bars indicate $\pm$ S.E. of oestradiol values.

when blood was collected every 6 hr after the onset of oestrus. The timing and brief duration of the pro-oestrous peak in progesterone concentration indicates that it could well be missed if blood samples were collected at less frequent intervals or if sampling were begun after the onset of oestrus.

The pro-oestrous rise in plasma progesterone precedes, by about 12 hr, the peak in plasma oestradiol found about 4 hr before the onset of oestrus. This suggests a possible synergistic effect of progesterone with oestradiol, which could influence the manifestation of oestrus and sexual receptivity. This has been found to occur in several species, including the guinea-pig, rat, mouse, hamster and in experimentally treated cows (Melampy, Emmerson, Rakes, Hanka & Eness, 1957) as well as in sheep (Robinson, 1954). Progesterone exhibits rather specific and differential influences on hypothalamic neurons (Cross & Silver, 1966) and it has been shown that, in ovariectomized hamsters, reflex mating activity could be induced when progesterone was injected directly into the right lateral ventricle of the brain (Kent & Liberman, 1949). It is worth noting that, in ovariectomized cows, injection of low doses of progesterone 12 hr before oestrogen, i.e. the same temporal relationship as found in the present study, resulted in a high incidence of manifestation of oestrus (Melampy *et al.*, 1957).

It is not surprising that the surge in progesterone concentration found in the present study is of moderate magnitude—only about 40% of the mean progesterone values (5.4 ng/ml) found during the luteal phase of the cycle (Shemesh *et al.*, 1971). A similar ratio of preovulatory to luteal phase (dioestrous) levels of progesterone has been reported in the cyclic hamster (Lukaszewska & Greenwald, 1970). A high level of progesterone might delay the onset of oestrus, as indicated by the finding of Melampy *et al.* (1957) that large doses of progesterone were antagonistic, rather than synergistic, to the action of oestrogen in inducing oestrous behaviour in ovariectomized cows. On the basis of this observation, these workers considered that the cessation of oestrous behaviour in the normal cow might be due to the antagonistic action of a presumed rise in progesterone concentration. This suggestion is not supported by the present findings of consistently low levels of progesterone from before the onset of oestrus to 24 hr afterwards, which is in accord with the results of Kazama & Hansel (1970).

In ovariectomized cows, oestrus can be induced by injecting oestrogen alone (Asdell, de Alba & Roberts, 1945). In sheep too, Robinson (1954) found that oestrogen alone was sufficient to induce an initial oestrus in ovariectomized ewes. In order to ensure good results in the induction of successive oestrus in the ewes, however, it was necessary to give an initial 'priming' treatment with progesterone before oestrogen.

The source of the pro-oestrous surge of progesterone is probably the adrenal glands. This assumption is based upon the following evidence: (a) the corpus luteum has clearly regressed by this time and is not producing progesterone; (b) the cow's ovary contains relatively little interstitial tissue which could respond to LH at this period; (c) concentrations of ovarian vein progesterone during the oestrous cycle of the cow are lowest around oestrus (Dobrowolski, Stupnicka & Domanski, 1968). By contrast, detectable levels of plasma progesterone have been noted in the ovariectomized cow (McCracken, 1963;

Shemesh, Ayalon & Lindner, 1968) and the adrenal gland has been shown to produce progesterone in the cow (Balfour, Comline & Short, 1957). The participation of progesterone of adrenal origin in influencing the onset of oestrus has been demonstrated in the rat (Feder, Brown-Grant & Corker, 1971).

The pro-oestrous surge in progesterone concentration found in this study occurs well before the ovulatory peak of LH in peripheral plasma in the cow, which has been reported to appear about the time of the onset of oestrus or shortly thereafter (Schams & Karg, 1969; Henricks *et al.*, 1970). This is in contrast to the situation in many other species (human: Neil, Johansson, Datta & Knobil, 1967; rat: Feder, Goy & Resko, 1967; hamster: Lukaszevska & Greenwald, 1970; guinea-pig: Feder, Resko & Goy, 1968; rabbit: Hilliard, Hayward & Sawyer, 1964), in which it has been demonstrated that the pre-ovulatory surge of progesterone occurs simultaneously with or after the peak level of LH.

In conclusion, it appears that the bovine may be included in the list of species in which a preovulatory rise in peripheral plasma progesterone concentration occurs. The primary effect of this surge seems to be to facilitate the manifestation of oestrus and sexual receptivity. In contrast to reports for other species, this peak occurs well before and not simultaneously with or after the pre-ovulatory LH surge.

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