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Effects of the ovarian steroid hormone profile on the endometrial EGF concentration
of the following estrous cycle in dairy cows

(乳牛における卵巣ホルモン濃度推移が次の発情周期での子宮内膜 EGF 濃度に及ぼす効果)

Endometrial epidermal growth factor (EGF) has been shown as an indicator of endometrial function and fertility in dairy cows. In fertile cows, the endometrial EGF concentrations peak twice, on days 2-4 and 13-14, with lesser concentrations of EGF around day 7 (day 0 = estrus). The decrease or loss of the peak has been linked to reduced fertility in repeat breeder (RB) cows and high-yielding cows. The two periods: (1) between luteolysis and estrus (or ovulation) and (2) early luteal phase may be essential to understand reduced fertility from the point of view of ovarian steroid hormones. Since the expression of EGF in the endometrium is primarily regulated by estradiol (E_2) and progesterone (P_4), changes in circulating E_2 and P_4 concentrations may be amplified in the endometrium as an altered EGF profile. Therefore, I hypothesized that an alteration of E_2 and/or P_4 in one of the critical periods from luteolysis to estrus or ovulation (Chapter 1) and in the early luteal phase (Chapter 2) may induce the loss or decrease of EGF peak concentrations and reduced fertility. In Chapter 1, I examined the effect of the timing of luteolysis induced by prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) administration in relation to the stage of follicular development on the profile of E_2 and P_4 between luteolysis and ovulation and EGF concentrations on day 3 of the following estrous cycle. Cows were treated with $PGF_{2\alpha}$ either on days 12 to 14 (selection phase group) or on days 16 to 17 of the estrous cycle (control group). Then, endometrial tissues were collected by biopsy on day 3 for EGF assays. Endometrial EGF concentration of cows with

both the normal and altered profiles was lower in the selection phase group than that in the control group ($P < 0.05$). The cows of the selection phase group showed lower conception rate than those of the control group ($P < 0.05$). In Chapter 2, I examined the effects of differing P_4 concentrations in the early luteal phase on the endometrial EGF concentration in the late luteal phase at the time of the second EGF peak and on day 3 of the following estrous cycle. Cows were either received an intravaginal P_4 device from day 5 to day 9 (day 0 = estrus, High P_4 group) or received $PGF_{2\alpha}$ treatments on days 3, 3.5 and 4 (Low P_4 group) or received no further treatment (Control group). Endometrial EGF concentrations were determined on day 14 of the cycle, and cows were allowed to show natural estrus. The endometrial tissue was obtained again on day 3 of the estrous cycle. On day 14, the proportion of cows that showed endometrial EGF concentrations lower than the lower limit of the normal range on day 14 was greater for Low P_4 compared with Control. On day 3 of the following estrous cycle, EGF concentrations in Low P_4 group were lower than those in High P_4 and Control groups ($P < 0.05$). The present study indicated that the alterations of E_2 and/or P_4 during different timing of estrous cycle in relation to the follicular developmental stages is one of the potential causes by which EGF concentrations in the following estrous cycle decrease and reduce fertility in the dairy cow.