Summary
Parturition can be synchronized in cattle by inducing or postponing. An intramuscular injection of glucocorticoid and/or prostaglandin F2α (PGF) induces calving within a few days after the treatment with a high incidence of retention of fetal membrane. A combined administration of a long-acting glucocorticoid and PGF improves the synchrony of parturition, but does not reduce the incidence of retained placenta. An attempt has been made to reduce the incidence of retention of fetal membrane by using a high dose of estradiol and a long-acting PGF analog without success. Night-time calving can be eliminated by postponing labor overnight with double administrations of such β2-adrenergic stimulants as isoxuprine, clenbuterol, and ritodrine. The postponement of parturition shows no adverse effect on cows and newborn calves. It is also possible to synchronize parturition in a narrower time frame by combining the induction and postponement. Further studies are needed to reduce the incidence of retention of fetal membrane following induced calving.

Key Words: cattle, induction of parturition, prostaglandin F2α, glucocorticoids, β2-adrenergic stimulants, retention of fetal membrane

Introduction
Advantages of planned parturition over spontaneous delivery may include saving time for observing and attending the parturition and preventing complications which may occur in unattended parturition. Controlling time of parturition to avoid night-time calving is also beneficial for providing colostrum to a newborn calf in time. Induction of parturition is also indicated to prevent dystocia caused by relative fetal oversize associated with prolonged gestation period or small pelvic size in heifers.

Parturition can be controlled by either shortening the gestation period or extending the period. In cattle calving can be successfully induced by an intramuscular injection of glucocorticoid or prostaglandin F2α (PGF). Time required from the treatment to calf delivery was reported to be between 24 and 72 hours, an average being 48 hours (BARTH et al., 1986). Following parturition induced with glucocorticoid or PGF, cows show a high incidence of retention of fetal membrane (BARTH et al., 1986), although no other harmful effects on dams and newborns have been reported. The high incidence of retention of fetal membrane as well as variability in intervals between treatment and calf delivery are major factors which limit an extensive use of
glucocorticoid and PGF for inducing parturition. About 60 % of calving occurs in the night time. The parturition can be postponed overnight in cows at the first stage of labor late in the afternoon by double administrations with β2-adrenoceptor stimulant (ARBEITER et al., 1980). When cows are already at the second stage of labor, the protocol is not effective to avoid night time calving. Isoxuprine and clenbuterol have so far been used for postponement of parturition. This paper aims to report possibilities to develop practical methods for inducing parturition with a low incidence of retention of fetal membrane and for postponing parturition over night based upon our experiments.

**Inducing Parturition with Long-acting Dexamethasone and PGF**

The occurrence of retention of fetal membrane following induced parturition is due largely to a delivery of fetus with premature placenta. Long-acting glucocorticoid is known to be effective to facilitate maturation of the placenta in cattle. Bo et al. (1992) reported that an administration of a long-acting glucocorticoid, dexamethasone trimethylacetate, 6 days prior to PGF injection at 270 days of pregnancy significantly reduced the incidence of retention of fetal membrane. Further field studies may be needed to establish practical methods for inducing calving without side effects.

Attempts have been made to develop the method using another long acting glucocorticoid, dexamethasone isonicotinate (DEX-I) (Asistar, Boeringer Ingelheim) for planned parturition which may allow Holstein-Friesian cows to calve at due dates, 280 or 281 days after insemination, without an increase in the incidence of retention of fetal membrane.

A total of 56 Holstein-Friesian cows in two herds were used. Thirty-seven cows in one herd due to calve during a period between December 1992 and July 1993 were divided into three groups; first group of 13 cows were injected intramuscularly with 21 mg DEX-I on 274 days of pregnancy at 18:00 hours, followed by an intramuscular injection with 500 μg cloprostenol (CLO) on 278 days at 22:00, second group of 9 cows were treated with CLOl alone on 278 days at 22:00, while third group of 15 cows were not given any treatment until their gestation periods exceed over 285 days and served as controls. The other 19 cows in another farm were divided into two groups at random. A group of 12 cows were injected with 21 mg DEX-I on 274 days and 500 μg cloprostenol on 279 days of pregnancy at 9:00.

Blood samples were collected via the tail vein daily from 273 days of pregnancy till the day of calving for determination of plasma concentrations of estrone sulfate and progesterone. In newborn calves blood was sampled via the jugular vein 2, 12, 24, 72, and 120 hours after birth to measure serum protein and gamma globulin concentrations.

**Synchronization of parturition with long-acting dexamethasone and PGF**

Of 25 cows treated with DEX-I on 274 days of pregnancy, 3 cows had already calved before the scheduled day for CLO injection. The other 22 cows were administered with CLO on 278 days at 22:00 and 21 (95 %) of the cows delivered calves on 280 or 281 days (Table 1).

Mean intervals between CLO injections and calf delivery were 34 ± 7 (SD) hours in DEX-I/CLO treated group, 34 ± 13 hours in CLO treated group, while the control group needed 127 ± 47 hours from 278 days of pregnancy at 22:00 to calf delivery.

On the other hand, in cows which were not given DEX-I and treated with CLO alone percentage of cows calved 280 or 281 days after last insemination was 62.5 %. Of the control animals, 6 cows calved on 275 to 278 days of pregnancy, Only one cow delivered a calf 280 days after insemination.
Table 1
Synchronization of parturition with a combined administration of dexamethasone isonicotinate (DEX-I) and clopostenol (CLO) in dairy cattle

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Day of CLO injection</th>
<th>No. of cows (275-278)</th>
<th>Day of calving</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEX-I CLO</td>
<td>278</td>
<td>13</td>
<td>10 1 0 0</td>
</tr>
<tr>
<td>DEX-I CLO</td>
<td>279</td>
<td>12</td>
<td>7 3 1 0 0</td>
</tr>
<tr>
<td>CLO</td>
<td>278</td>
<td>9</td>
<td>5 3 1 0 0</td>
</tr>
<tr>
<td>CLO</td>
<td>279</td>
<td>7</td>
<td>1 3 3 0 0</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td>15</td>
<td>0 1 0 6 2</td>
</tr>
</tbody>
</table>

(*) Number in parentheses shows cows that calved before CLO injection.

Retention of fetal membrane

The incidence of retention of fetal membrane was 75% in DEX-I and CLO treated group, 60% in CLO alone treated group and 26% in the control group.

Fig. 1: Serum concentrations of estrone sulfate in cows with retention of fetal membrane (RFM)

In DEX-I/CLO treated group cows with retention of fetal membrane showed significantly lower serum estrone sulfate concentrations before parturition than those which expelled fetal membrane within 12 hours after calving (P<0.01)(Fig. 1). No significant increase in serum estrone sulfate concentrations was shown after a DEX-I injection. The significantly lower serum concentrations of estrone sulfate were also seen in both CLO treated and control groups (P<0.01).

Serum protein and gamma-globulin concentrations in newborn calves

Serum concentrations of total protein and gamma-globulin in newborn calves at 24 hours after birth were 5.0 ± 0.2 g/dl and 0.9 ± 0.07 g/dl in DEX-I/CLO treated group, 5.6 ± 0.3 g/dl and 0.89 ± 0.13 g/dl in CLO group, and 5.0 ± 0.2 g/dl and 0.89 ± 0.13 g/dl in the control group.

Changes in serum gamma-globulin concentrations in calves after induced or spontaneous parturition are shown in Fig. 2. There was no significant difference in the mean values among the three different groups.

Results of this study showed that a combined administration of a long-acting glucocorticoid, DEX-I and an analog of PGF, CLO at 4 or 5 days interval was effective
to reduce the variation in time between treatment and parturition. Almost all cows calved on 280 or 281 days of pregnancy. This agrees with the earlier report by BO et al. (1992) who injected with another long-acting glucocorticoid, dexamethasone trimethylacetate on 270 days of pregnancy, followed by PGF and a short-acting glucocorticoid on 276 days in beef cattle.

The incidence of retained placenta in DEX-I/CLO group was significantly higher than the figure in the control group. No significant difference in the incidence was shown between DEX-I/CLO and CLO groups. Long-acting glucocorticoids are known to facilitate maturation of the placenta (BO et al., 1992; GRUNERT et al., 1989) and, therefore, are considered to be effective to reduce the incidence of retention of fetal membrane. In our study, however, DEX-I was neither effective in maturation of the placenta nor in reduction of retention of fetal membrane. Insufficient effect of DEX-I on the placental maturation indicated by a lack of response of serum estrone sulfate concentrations after DEX-I injection might have attributed to the failure in reducing the incidence of retention of fetal membrane.

Cows with retention of fetal membrane showed significantly lower serum estrone sulfate concentrations than those which expelled the placenta normally in the present study. It is likely that inducing parturition in cows with premature placenta indicated by low estrone sulfate levels is a cause of retention of fetal membrane.

RAMUSSEN et al. (1995) later reported that a high dose of estradiol in conjunction with a long-acting PGF analog did not reduce the incidence of retention of fetal membrane.

From a practical point, adequate treatment for retention of fetal membrane to minimize the complications should be recommended rather than prevention of retained placenta after induced parturition.

In conclusion a combined use of a long-acting glucocorticoid and PGF is effective to synchronize parturition at predictable days and has no adverse effects on dams and newborns, although the treatment may not be effective to facilitate placental
maturation to an extent enough to reduce the incidence of retention of fetal membrane.

**Delaying Parturition with β2-Adrenoceptor Stimulant to Reduce Night-Time Calving**

Use of such β2-adrenoceptor stimulants as clenbuterol and isoxuprine which stimulate the β2 receptors of uterine muscle cells has been shown to be effective in postponing labor and eliminating night-time calving (ARBEITER et al., 1980). No adverse effects of postponing labor on the course of parturition, expulsion of afterbirth, viability of calves have been reported. Results of our study also indicated that double administrations of clenbuterol at 18:00 and 22:00 are effective to eliminate night-time calving and the treated cows have lower incidences of dystocia and retention of fetal membrane and a higher first service conception rate than controls (NAKAO et al., 1992). The treatment did not adversely affect milk yield.

Ritodrine hydrochloride, the second generation β2-adrenoceptor stimulant, can be also used for postponing calving (Table 2) (NAKAO et al., 1993).

<table>
<thead>
<tr>
<th>Stage of labor at 18:00</th>
<th>Time (18:00)</th>
<th>Nighttime calving (%): Treated</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{st} stage</td>
<td>23</td>
<td>4.2</td>
<td>66.7</td>
</tr>
<tr>
<td>2\textsuperscript{nd} stage</td>
<td>12</td>
<td>29.4</td>
<td>0</td>
</tr>
<tr>
<td>Prepartum</td>
<td>23</td>
<td>9.4</td>
<td></td>
</tr>
<tr>
<td>Total (expect controls)</td>
<td>46</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Calving can be better synchronized by postponing parturition with clenbuterol after inducing it with glucocorticoid and/or PGF (Table 3).

Table 3

<table>
<thead>
<tr>
<th>Protocol for synchronization of calving by induction and postponement in combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>274 d DEX-I</td>
</tr>
<tr>
<td>18:00 Check cervical dilation</td>
</tr>
</tbody>
</table>

In Holstein-Friesian cattle DEX-I is injected on 274 days of pregnancy and then CLO is given on 278 days at 22:00. On the following day at 18:00 cows are checked for the dilation of the cervix and clenbuterol is given to cows in the first stage labor first at 18:00 and again at 22:00 to postpone calving overnight. Almost all cows deliver calves in day time the following day. Cows which are already in the second stage labor are not given clenbuterol, because they are expected to calve before mid-night on the same day. According to our experiments, all cows administered double doses of clenbuterol calved on the following day after 5:00 in the morning.

Parturition can be synchronized within a narrow time frame by inducing with glucocorticoid and/or PGF and postponing with β2-adrenoceptor stimulants. However, so far no reliable methods to synchronize parturition without causing a high incidence of retention of placenta are available for practical application. Further studies are needed for developing the novel method for inducing parturition without side effects in cattle.
References


Author's address

PROF. TOSHIHKO NAKAO, DVM, MS, PhD
Department of Animal Resources Development
Graduate School for International Development and Cooperation
Hiroshima University
Higashi-Hiroshima 739-8529, Hiroshima, JAPAN

E-Mail: nakao@hiroshima-u.ac.jp