*Therapeutic and Feedlot Abortion Application of Prostaglandins

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Introduction

It is now well established that natural prostaglandin (PFG2α), administered by various routes can induce functional and morphological regression of the corpus luteum (luteolysis) in a wide variety of species. Rowson, *et al.* (1972), reported that $PGF_{2\alpha}$ (0.5 mg given on two consecutive days) would induce luteolysis in cattle when administered locally into the uterine horn adjacent to the ovary bearing the corpus luteum. Since that time further work has shown $PGF_{2\alpha}$ to be luteolytic in cattle at much higher single doses by the intramuscular, subcutaneous and intravaginal routes (Oxender, *et al.* 1974).

A new series of compounds, the 16-aryloxy-prostaglandins, have now been synthesized (Binder, *et al.*, 1974) and tested in a number of species. Dukes, *et al.* (1974), demonstrated that several of these compounds are extremely potent luteolytic agents and highly selective in their pharmacological activity. This selectivity gives them a very wide margin of safety in domestic species. One of these compounds, cloprostenol (ICI 80,996), is luteolytic in cattle at a single intramuscular dose of 500 μg (Cooper and Furr, 1974).

Cloprostenol and $PGF_{2\alpha}$ are being used extensively in a number of countries to control reproduction and synchronize estrus in cycling cattle. Generally two single injections are given, separated by 10-12 days to overcome the insensitivity of the corpus luteum early (first 4-5 days) in the cycle. This regime of treatment is followed by a synchronized heat of normal fertility (Inskeep, 1973; Cooper, 1974; Lauderdale, 1975; Oxender, 1975; Bailie and Dury, 1976; Hearnshaw, 1976).

The practicing veterinarian frequently encounters several reproductive problems in cattle associated with persistence of luteal function which luteolysis and induction of estrus will help to resolve, e.g., pyometra, mummified or macerated fetus, ovarian luteal cysts and unwanted pregnancy. Also, many cows not detected in estrus (sub-estrus) are normal cycling animals which for various reasons (management deficiencies and variations in time and intensity of estrus) are not caught in heat during the desired breeding period. A single intramuscular dose of 500 μg cloprostenol has been demonstrated to be effective in treating these conditions (Cooper, et al., 1976; Day, 1976; Jackson and Cooper, 1976; Eddy, 1977; Jackson, 1977; Jackson, 1977). This paper presents the results of United States and Canadian field trials conducted for the purpose of evaluating the therapeutic value of cloprostenol.

1. Sub-estrus (no visible estrus)

This condition occurs particularly in heavy-yielding dairy cows at or near the time of peak lactation. The animals usually have normal ovarian cyclicity but the behavioral manifestations of estrus are either mild (and therefore difficult to detect) or absent. The failure to detect estrus in such animals and therefore to inseminate them, leads to an extension of the calving interval and consequently reduced efficiency and increased economic losses.

Seguin, *et al.* (1977), conducted two trials involving 24 dairy herds in which fertility examinations were performed on a regular basis. Animals were eligible for these trials if they had not been detected in estrus since the last visit, the reproductive tract was found to be normal and a palpable corpus luteum was present on either ovary. In the first trial animals were injected with either 500 μg cloprostenol I.M. or 2 ml saline I.M. as a placebo. All animals were to be bred at the first detected estrus following treatment. The farmers did not know which animals received cloprostenol and which ones received the saline. In the second trial animals were selected in the same manner as for the first trial. However, in this trial all cows were treated with cloprostenol (500 μg given I.M.) and inseminated either upon detection of estrus or at a fixed time of 72 and 96 hours following injection without regard for signs of heat.

The results for the first trial are presented in Table I. A total of 181 cases were placed on trial with 98 animals receiving cloprostenol and 83 serving as controls. By Day 5, 66% of the cloprostenol treated animals were detected in estrus while only 13% of the saline controls were observed in heat. This difference is statistically significant ($P < 0.01$). After 21 days the percent inseminated was similar for both groups. The conception rate (no. pregnant/no. bred) for both groups was the same (44%) during this 21 day period. Most of the cloprostenol treated animals detected in estrus were bred during the first five days following treatment. As a result, a significantly higher percentage of cloprostenol treated cows were pregnant within five days of treatment (31% vs. 5%, $p < 0.01$).

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Table I

Estrus and Fertility in Dairy Cows with Unobserved Estrus Treated with Cloprostenol (ICI 80,996) or with Placebo.

	Treatments	
	CP*	Saline
No. Treated	98	83
Percent Inseminated		
in 5 days	66**	13**
in 21 days	74	66
Conception Rate	44%	44%
Percent of Total Pregnant		
in 5 days	31**	5**
in 21 days	33	29

*500 μg cloprostenol (ICI 80,996) IM.
**P < .01

Table III

Clinical Response of Cattle Treated For Pyometra Comparing Cloprostenol (ICI 80,996) With Conventional Treatment

	Conventional Treatment	Cloprostenol
No. on trial	69	200
No. complete responses	41 (59.4%)***	176 (88.0%)***
No. partial responses	11 (15.9%)	12 (6.0%)
No. failures	17 (24.6%)***	12 (6.0%)***
No. bred and examined for pregnancy	25	96
No. pregnant (all breedings)[1]	17 (68.0%)	62 (64.6%)

***Cloprostenol treated significantly different from conventional treatment; P < 0.001.

[1]Based on available follow-up information since breeding and pregnancy results were not available for all cases. This does not reflect number of breedings per conception since some animals were bred more than once.

This trial demonstrates that cloprostenol is effective for inducing estrus in sub-estrous cattle and that fertility of the induced estrus is not different from the fertility of natural occurring estrus.

In the second trial 165 cows were treated with cloprostenol with 78 assigned to be bred upon detection of estrus and 87 animals to be bred at 72 and 96 hours following treatment. The results are given in Table II. Since not all animals were detected in estrus in the group designated to be bred at estrus, a significant advantage was demonstrated for fixed time insemination when comparing the percentage of animals inseminated in five days (60% vs. 98%; P < 0.01).

The conception rate was also higher in the group bred at 72 and 96 hours (59% vs. 40%; P < 0.05). Consequently, a higher proportion of animals conceived within five days of treatment in the fixed time insemination group (55% vs. 24%; P < 0.01). This trial suggests that the best approach to treating subestrus is to eliminate heat detection entirely and breed at a fixed time of 72 and 96 hours following cloprostenol treatment. Acceptable results can only be obtained, however, if accurate rectal examination is performed before treatment to establish the presence of a mature corpus luteum and a normal reproductive tract.

Table II

Reproductive Performance of Dairy Cows Treated for Unobserved Estrus with Cloprostenol (ICI 80,996) and Inseminated at Estrus or by Appointment.

	CP* & AI	
	at estrus	at 72 & 96 hours
No. Treated	78	87
Percent Inseminated in 5 days	60**	98** (87% per schedule)
Conception Rate	40%***	59%***†
Percent of Total Pregnant in 5 days	24**	55**

*500 μg cloprostenol (ICI 80,996) IM.
**P < .01
***P < .05
†For those bred per schedule.

2. Pyometra (Chronic Purulent Endometritis)

In this trial cloprostenol was tested as a treatment of pyometra. Animals were entered into this study if, the rectal examination revealed (1) no pregnancy, (2) fluid within the lumen of the uterus, and (3) a corpus luteum was present. Animals were assigned to a cloprostenol treatment group or a conventional therapy group as each case was encountered. Two hundred animals were treated with 500 μg cloprostenol intramuscularly while 69 control animals were treated with the drug routinely used for this condition by the clinical trialist. The control treatment used was usually an estrogen, which was administered intramuscularly.

The results for the pyometra treatments are given in Table III. In the cloprostenol treated group 88.0% of the animals responded with complete evacuation of the uterus while 59.4% of the control animals responded completely. Only 6.0% of the cloprostenol treated group failed to respond at all, while 24.6% in the control group had no response. These differences are statistically significant (P < 0.001). Follow-up breeding information which was available revealed 62/96 (64.6%) pregnant in the cloprostenol treated group and 17/25 (68.0%) pregnant in the control group.

3. Removal of Mummified or Macerated Fetus

The efficacy of cloprostenol for the treatment of mummified or macerated fetus was evaluated in this trial. The results for the animals treated are presented in Table IV. Thirty-eight cases were placed on trial and 29 (76.3%) responded with evacuation of the fetus from the uterus. As is often the case in induced abortion of a mummified or macerated fetus, manual removal of the fetus from the vagina was required for several animals. Fourteen animals were bred following successful abortion and 11 (78.6%) are known to be pregnant following one or more breedings.

4. Treatment of Ovarian Cystic Degeneration (luteal cysts)

One form of cystic degeneration of the ovaries in the bovine develops as a result of the failure of ovula-

Table IV
Clinical Response of Cattle Treated for
Unwanted Pregnancies, Mummified or Macerated Fetus
and Luteal Cysts with Cloprostenol (ICI 80,996)

Diagnosis	No. on Trial	Gestation State (Range-Days)	Positive Response	Subsequent[1] Breeding No. Pg/No. Bred
Mummified or Macerated Fetus	38	-	29 (76.3%)	11/14 (78.6%)
Luteal Cyst	18	-	17 (94.4%)	14/15 (93.3%)
Unwanted Pregnancy	82	35-140	80 (97.6%)	16/16 (100%)

[1]Based on available follow-up information since breeding and pregnancy results were not available for all cases. This column does not reflect number of breedings per conception since some animals were bred more than once.

tion with the resulting follicle becoming cystic and partially luteinized. This trial was conducted to determine if cloprostenol could be used effectively to regress luteal cysts. Diagnosis was based on the animal being clinically anestrus with rectal examination findings of a thick walled cystic structure on either ovary with a normal uterus present.

Eighteen cases of luteal cysts were treated with cloprostenol and the results are presented in Table IV. At the examination subsequent to treatment, 17 of the 18 cases (94.4%) had responded by regression of the cystic structure. Fifteen of the animals were subsequently bred with 14 (93.3%) being confirmed pregnant.

5. Treatment of Normal but Unwanted Pregnancies

Maintenance of pregnancy in the bovine is known to be dependent upon luteal progesterone until an ill-defined stage of gestation around the 150th day. Since cloprostenol is a potent luteolytic agent, it can be used effectively to terminate pregnancy during the first five months of gestation. In this trial 82 cases of unwanted pregnancy were treated with cloprostenol and the results are presented in Table IV. The stages of gestation ranged from 35 to 140 days. Eighty of the 82 (97.6%) cases responded with evacuation of the fetus. The abortions were uncomplicated and most occurred during the first six days post-treatment. In most cases membranes were delivered with the fetus.

6. Feedlot Abortion Application

Pregnancy in heifers entering feedlots is a well known cause of economic loss since it interferes with the growth of the heifer whose carcass is downgraded at slaughter. Three studies were conducted to determine the minimum effective dose of cloprostenol to cause abortion in feedlot heifers pregnant less than 150 days. Three hundred and fifty-six feedlot heifers were treated with 62.5 μg to 500 μg of cloprostenol. Abortion rates of over 94% were attained at dose levels of 375 μg and 500 μg. At 62.5 μg, 59.3% of the heifers aborted. These trials would suggest that 375 μg of cloprostenol can be used effectively to abort feedlot heifers under 455 kg (1,000 lbs.) up to five months of gestation.

Conclusions

The data presented clearly illustrates the immense potential and opportunity for the beneficial use of prostaglandins. This opportunity is accompanied by an equally high potential for misuse. As cattle prostaglandins become commercially available in the United States the veterinary profession will be charged with the responsibility of insuring proper usage. For therapeutic indications an accurate diagnosis must first be established based on careful and complete rectal examination of the entire reproductive tract. It is essential to remember that prostaglandins are effective only if a mature corpus luteum is present. When the prostaglandins are used to synchronize large groups of cattle, evaluation of the entire management system is necessary. There must be an adequate post-partum interval and the cattle must be cycling for prostaglandins to be effectively used. This again may mean careful evaluation of the reproductive tract by rectal palpation. A high plane of nutrition is also important both before and after the cattle are bred. Veterinarians who are equipped with proper palpation skills and knowledge of reproductive physiology will be able to use prostaglandins to successfully implement new and innovative management programs for their dairy and beef clients.

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