

The effects of treatment with cloprostenol or dinoprost within one hour of induced parturition on the incidence of retained placenta in cattle

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Abstract

Two experiments were designed to determine whether prostaglandin treatment within one hour postpartum would reduce the incidence of retained placentas after induction of parturition in beef cattle. In the first experiment, 70 cows were induced on day 276–278 of gestation with the combination of 500 µg cloprostenol and 25 mg dexamethasone (CP + Dex). Within one hour after parturition, cows received either 500 µg CP or 25 mg of dinoprost (DI). The incidence of retained placenta (RP) was 64.3% in induced groups and 0% in noninduced control cows and postpartum treatment with either CP or DI had no effect on placental retention.

A second experiment, utilizing 132 cows and heifers, was conducted to determine whether induction with Dex alone, rather than with CP + Dex, would influence the rate of placental retention after postpartum treatment with either CP or DI. The incidence of retained placenta ranged from 28.5 to 58.3% in induced females but was 0% in noninduced control females. As in the first experiment, postpartum prostaglandin treatment had no effect on placental retention.

The results of these experiments do not support the use of prostaglandins within one hour of induced parturition to reduce the incidence of retained placentas.

Résumé

Les effets d'un traitement avec le cloprostenol ou le dinoprost, administré durant la première heure suivant l'induction de la parturition, sur l'incidence de la rétention placentaire chez les bovins

Deux protocoles ont été élaborés afin de déterminer si un traitement avec des prostaglandines, administré durant la première heure postpartum, pourrait diminuer l'incidence de la rétention placentaire chez les bovins de boucherie dont la parturition aurait été provoquée. La parturition a été induite chez 70 vaches entre les 276 et 278^{ème} jours de gestation avec 500 µg de cloprosténol et 25 mg de dexaméthazone (CP + Dex).

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Durant l'heure qui a suivi la parturition, les vaches ont reçu soit 500 µg de CP ou 25 mg de dinoprost (DI). L'incidence de la rétention placentaire a été évaluée à 64,3 % pour le groupe dont la parturition a été induite et de 0 % pour un groupe témoin d'animaux dont la parturition n'a pas été provoquée. Le traitement postpartum avec soit du CP ou du DI n'a eu aucun effet sur l'incidence de la rétention placentaire.

Un deuxième protocole a été élaboré pour déterminer si l'induction de la parturition avec seulement de la dexaméthazone pourrait influencer le taux de rétention placentaire suite à un traitement postpartum avec soit du CP ou du DI. Cent trente-deux vaches ont été sélectionnées pour l'expérience. Le taux d'incidence de la rétention placentaire a varié de 28,5 à 58,3 % chez les vaches dont la parturition a été provoquée, mais a été de 0 % pour les vaches du groupe témoin dont la parturition n'a pas été induite. Le traitement postpartum aux prostaglandines n'a pas eu d'effets sur l'incidence de la rétention placentaire. Les résultats de ces expériences n'appuient pas l'utilisation des prostaglandines durant la première heure postpartum lors de parturition induite pour diminuer l'incidence de la rétention placentaire.

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Introduction

It is generally believed that parturition is the culmination of a cascade of endocrine events initiated by increased fetal adrenal cortisol secretion associated with maturation of the fetal hypothalamus-pituitary-adrenal axis (1). Maternal plasma cortisol does not parallel the peak seen in the fetal compartment and does not appear to be of the same importance as the fetal plasma levels, which rise from about 5 ng/mL at 20 days prepartum to about 70 ng/mL on the day of calving (2). It appears that fetal cortisol gradually reduces placental progesterone production (3), increases estrogen production in the cotyledon (2,4,5), and finally initiates the release of prostaglandin F₂ alpha (PGF) from the placentome. Complete luteolysis occurs in response to PGF release, and loss of progesterone support for the pregnancy results in parturition (4–7). Hormones used to induce parturition initiate the endocrine events triggered by fetal cortisol. Studies designed to develop effective methods for the induction of parturition in beef and dairy cattle have been underway for over two decades (8). Some of the more widely used short-acting induction agents include synthetic glucocorticoids (7–14), PGF (15–19), or a combination of these drugs (20–23).

Ideally, the induction of parturition should result in a reliable and predictable time period from treatment to fetal delivery, no placental retention, no adverse effects on cow or calf health, and no decrease in postpartum fertility (4). None of the presently available methods of induction fulfill all of the above criteria. When injections of glucocorticoids or PGF alone are given up to two weeks before normal term, efficacy is reported to be as low as 80%, with a considerable amount of variation in the treatment-to-calving interval (8,12,24). When dexamethasone (Dex) and PGF are given in combination, efficacy is 100%, with considerably less variation in treatment-to-calving interval (20,24). Regardless of the method used, a high incidence of placental retention occurs (7,18,20).

There is generally great concern about retained placenta in cattle, especially in dairy cows. However, some reports indicate that, with placental retention after induction of parturition, effects are not significant on uterine involution, resumption of cyclicity, postpartum fertility, pregnancy rate, or calving interval in either dairy or beef cows (7,12,18,25-28).

Attempts have been made to reduce the incidence of placental retention by using various estrogen preparations (27,29-34), oxytocin (35), dimenhydrinate (36), or relaxin (37) in conjunction with short acting induction agents. Long acting corticosteroids such as dexamethasone trimethylacetate have also been used to induce parturition and have resulted in a low incidence of placental retention; however, calf mortality due to prematurity and hypogammaglobulinemia was extremely high (38,39).

A markedly reduced incidence of placental retention has been reported when cows that were induced to calve with dexamethasone were treated with PGF (dinoprost) within one hour postpartum (40). However, the possible role of PGF in placental release is not clear. One study indicated that prepartal placental concentrations of PGF decreased in cows that retained the placenta (41), but other studies have reported increased prepartal concentrations of PGF metabolite in the peripheral blood (42). In addition, some studies reported lower PGF synthesis in the early postpartum period of cows that retained fetal membranes (41,43), but others report increased PGF synthesis after calving in cows with retained placentas (44).

In cows calving spontaneously, PGF injections do not affect uterine motility significantly whether given before or after oxytocin treatment (45). In that study, no significant differences in uterine contractility were observed at one and six hours postpartum in cows induced to calve, and in cows calving spontaneously. In these same cows, uterine motility did not differ between cows retaining and not retaining the placenta at one and six hours postpartum; however, cows with retained placentas had greater uterine contractility at 48 hours postpartum (46). Thus, the placental retention was not a result of the lack of uterine contractility during the early hours of the postpartum period.

We report herein the results of two experiments that were designed to determine whether treatment within one hour postpartum with either of two different prostaglandins (dinoprost or cloprostenol) would

reduce the incidence of retained placenta in cows induced to calve.

Materials and methods

Experiment 1

One hundred-and-three Hereford and Hereford X Angus crossbred cows from a University of Saskatchewan beef research herd were used in this trial. Stages of pregnancy were determined by transrectal palpation six weeks after the end of a 60 day breeding season and compared with breeding observations made at dawn and at dusk over the first 30 days. On days 276-278 of gestation, cows were placed randomly by replicate into one of four treatment groups. Groups I, II, and III were induced to calve with 500 µg cloprostenol (CP) (Estrumate, Coopers Agropharm Inc., Ajax, Ontario) and 25 mg dexamethasone (Dex) (Dexamone "2", rogar/STB, BTI Products Inc., London, Ontario) administered concurrently at different IM injection sites. Group IV was designated as a noninduced control group. Within one hour after parturition, cows in group I received 2 mL of saline, cows in group II received 500 µg CP, and cows in group III received 25 mg dinoprost (DI) (Lutalyse, The Upjohn Company, Orangeville, Ontario). All postpartum treatments were given IM. Placentas were considered retained when they remained in the uterus for more than 24 hours after calving. Cows with retained placentas were treated IM with antibiotics if they became inappetent or had rectal temperatures greater than 39.5°C.

End points to be recorded were induction success rate, time from induction treatment to completion of delivery, calving ease, calf vigor, incidence of retained placenta, duration of placental retention, first service conception rate, and pregnancy rate. Calf vigor was considered normal if the calf was able to stand and nurse within one hour of birth.

Experiment 2

The second experiment was designed to confirm the results of experiment 1 and to determine whether a postpartum PGF treatment after induction of parturition with Dex alone, rather than with CP and Dex, would reduce the incidence of placental retention.

Eighty-eight cows and 44 heifers of Hereford and Hereford X Angus breeding were used in this experiment. As in experiment 1, stages of pregnancy were determined by transrectal palpation and compared with breeding observations over the first 30 days of a 60 day breeding season. Cows and heifers were placed at random into one of seven groups. Groups I to VI were induced to calve on day 276-278 of gestation. Groups I, II and III received 500 µg CP and 25 mg Dex concurrently at separate IM injection sites. Groups IV, V and VI received 25 mg Dex alone. Group VII (control) received no treatment. Cows were placed in groups in such a way that, for every cow induced with the combination of CP and Dex, two cows were induced with Dex alone. All induction drugs were given IM at 1200 hours. Cows calving less than 24 hours after induction treatment were considered to have calved naturally and cows not calving by 72 hours

Table 1. Placental retention (RP) in cows induced to calve with a combination of cloprostenol (CP) and dexamethasone (groups I, II and III) and treated within one hour of parturition with CP, dinoprost (DI), or saline. (Experiment 1)

Group	Postpartum treatment	Number of cows	RP (%)	Duration of RP (hours, $\bar{X} \pm \text{SEM}$)
I	CP	23	65.2	79.0 ^a ± 15.4
II	DI	24	58.3	86.8 ^a ± 17.4
III	Saline	23	69.5	96.2 ^a ± 16.3
IV	Control	33	0.0	3.0 ^b ± 0.2*

^{ab}Means with different superscripts are different ($p < 0.01$)

*Physiological time for expulsion of membranes in normal cows

after induction treatment were considered to be induction failures. Cows considered as induction failures were placed in the control group.

Within one hour postpartum, cows in groups II (CP + Dex-CP) and V (Dex-CP) received 500 µg cloprostenol, cows in groups III (CP + Dex-DI) and VI (Dex-DI) received 25 mg dinoprost, and cows in groups I (CP + Dex) and IV (Dex) received 2 mL saline and served as induction controls.

Blood samples were taken daily at 1200 hours by venipuncture of the coccygeal vessels from the time of induction treatment until three days after parturition from five animals selected at random from each group. Serum was harvested by centrifugation within 30 min of collection and stored at -20°C until assayed for progesterone, estradiol 17β, and cortisol by radioimmunoassay (15,47). Serum hormone levels were compared between groups relative to the time of calving and placental expulsion. End points recorded were induction success rate, time interval from injection to completion of delivery, calving ease, calf vigor, incidence of retained placenta, duration of placental retention, subsequent first service conception rate, and pregnancy rate. Cows which retained their placenta were monitored closely for depression, anorexia, and fever. Systemically ill cows with rectal temperatures greater than 39.5°C were treated IM with antibiotics.

Data were analyzed with the general linear models procedure (GLM) of the Statistical Analysis System (SAS) (48). The differences between experimental groups and treatment means for the interval from induction to calving were tested using Student's *t*-test under the assumption of unequal variances. The times from calving to placental release were not distributed normally. Therefore, in order to detect differences between treatment groups, the data were first normalized using rank transformation. A one-way analysis of variance was performed upon the ranks, and differences between pairs of mean ranks were tested using the least significant difference method. Frequencies of placental retention, first service conception, and pregnancy were analyzed by Chi square.

Results

Experiment 1

All induced cows (CP + Dex) calved within 48 hours of treatment ($\bar{X} \pm \text{SEM} = 35.5 \pm 0.7$ h). The

incidence of retained placenta (Table 1) ranged from 58.3–69.5% in the induced groups; placentas were not retained by cows in the control group IV. The duration of placental retention ($\bar{X} \pm \text{SEM}$) in induced groups ranged from 79.0 ± 15.4 h to 96.2 ± 16.3 h, but time to expulsion of membranes was only 3.0 ± 0.2 h in control cows. There were no significant differences among treated groups in the incidence or duration of placental retention. However, incidence and duration of placental retention in all induced groups were significantly greater than in the control group IV ($p < 0.01$).

All calves were healthy at birth and there were no calf losses within the first 10 days after birth. Birth processes were considered to be normal and there were no differences among groups in the degree of assistance required.

There was no reduction in the incidence of placental retention due to PGF treatment within one hour after calving. However, retained placenta did not cause any serious medical complications or reduction in fertility. Observations in the subsequent 60 day breeding season and pregnancy testing showed no differences in first service conception rates (67.6% and 69.7%) or pregnancy rates (84.0% and 94.0%) in cows that retained or did not retain the placenta, respectively ($p > 0.3$).

Experiment 2

Similar results in the success rate of induction were seen for cows induced with the combination of CP + Dex and with Dex alone (97.2% and 96.9%, respectively). Cows treated with CP + Dex calved within 60 hours ($\bar{X} \pm \text{SEM} = 38.6 \pm 1.1$ h) and cows treated with Dex alone calved within 70 hours ($\bar{X} \pm \text{SEM} = 43.7 \pm 1.3$ h). The interval from treatment to calving was significantly shorter for cows induced with CP + Dex than cows induced with Dex alone ($p < 0.01$).

The incidence of retained placenta among induction treatment groups ranged from 28.5%–58.3% ($p = 0.44$) and the mean duration of placental retention in these groups ranged from 41.4–84.1 h. The differences between induced groups were not significant ($p > 0.1$, Table 2). There were no retained placentas in the control group VII and the mean interval to expulsion after parturition in this group (3.7 h) was significantly less

Table 2. Induction success rate, interval from treatment to calving (mean + SEM), incidence of retained placenta, and duration of placental retention (mean + SEM) in cows induced to calve with cloprostenol and dexamethasone in combination (CP + Dex) or dexamethasone (Dex) alone

Treatment	Induction success (n)	Interval to calving (h) ¹	Retained placenta (%)	Duration of retention (h)
CP + Dex	9/10	39.7 ± 2.0	30.0 ^a	54.6 ± 25.3 ^a
CP + Dex-CP ²	14/14	37.2 ± 1.7	35.7 ^a	73.9 ± 28.9 ^a
CP + Dex-DI ³	12/12	38.9 ± 2.3	58.3 ^a	73.8 ± 19.0 ^a
Dex	21/21	41.3 ± 1.9	28.5 ^a	41.4 ± 15.1 ^a
Dex-CP ²	22/23	44.6 ± 2.5	52.2 ^a	84.1 ± 18.9 ^a
Dex-DI ³	21/22	45.2 ± 2.4	45.5 ^a	76.6 ± 21.3 ^a
Control	0/30	NA ⁴	0.0 ^b	3.7 ± 0.4 ^b

¹Induction failures removed

²Cows received CP within one hour after calving

³Cows received DI within one hour after calving

⁴Not applicable

^{ab}Percentages and means in columns with superscripts not in common are significantly different ($p < 0.01$)

than for the induced groups ($p < 0.01$). Twenty-four of 43 cows which retained the placenta (55.8%) had elevated rectal temperatures ($> 39.5^{\circ}\text{C}$) by 48 hours postpartum and were treated IM with antibiotics for two to five days. In addition, one cow with a rectal temperature of less than 39.5°C received antibiotic treatment. In the following breeding season, cows which retained the placenta had a first service conception rate of 56.1% (23/41) versus 76.7% (66/86) for cows not retaining the placenta ($p = 0.03$). The pregnancy rate of cows which retained the placenta was 75.6% (31/41) versus 91.7% (79/86) for cows not retaining the placenta ($p = 0.025$). Interestingly, cows which received antibiotic treatments had numerically lower first service conception rates and lower pregnancy rates than cows which retained the placenta but did not receive antibiotics; however, the differences were not significant ($p > 0.7$).

In all groups the mean progesterone concentration was 4.0 ± 0.2 ng/mL 48 hours before parturition. Significant and precipitous declines in progesterone concentrations occurred between 48 and 24 hours before calving in all cows whether or not they subsequently retained the placenta. Progesterone concentrations decreased to less than 1 ng/mL on the day of calving and mean values postpartum never exceeded 1 ng/mL in any group (Figure 1).

In noninduced cows, the peripheral serum cortisol concentrations gradually increased before parturition, reaching mean peak concentrations of 14 ng/mL at parturition, and then declined after parturition (Figure 2). In all induced groups, mean cortisol concentrations ranged from 9–12 ng/mL 48 hours before calving, followed by a significant and rapid decline 24 hours before parturition. Starting from day 1 postpartum, the cortisol concentrations in induced cows gradually increased to peak on day 2 after parturition. Cortisol levels tended to be higher on day 2 postpartum in cows retaining than in cows not retaining their placenta; however, the differences were not significant ($p > 0.05$).

In all groups, serum estradiol levels increased rapidly to mean peak concentrations of 230 pg/mL 24 hours before parturition, followed by a precipitous fall near the time of calving and a subsequent gradual decline to concentrations of 10 pg/mL 48 hours after calving (Figure 3). In cows which did not retain the placenta, estradiol levels began to decline 24 h prior to parturition, whereas, in cows which retained the placenta, estradiol levels did not begin to decline rapidly until the time of parturition.

As in experiment 1, there were no unusual complications in any of the treatment groups. However, two dystocias were recorded (one a fetal-maternal disproportion and the other a posterior presentation). One calf from an induced cow and one calf from a noninduced cow died from coliform septicemia and one cow which had retained her placenta died five days after parturition of septic metritis (confirmed by postmortem examination).

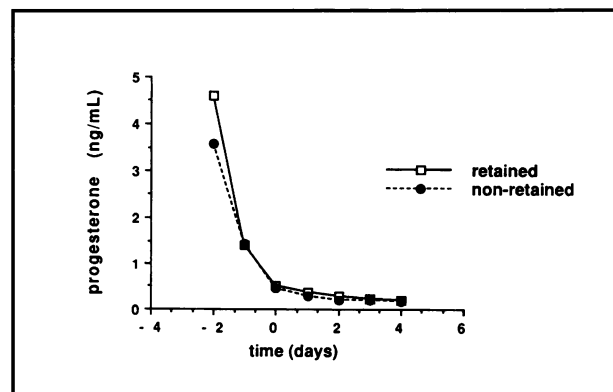


Figure 1. Mean peripheral concentrations of progesterone in cows retaining or not retaining the placenta after induction of parturition with cloprostenol and dexamethasone in combination, or with dexamethasone alone. Calving occurred on day 0.

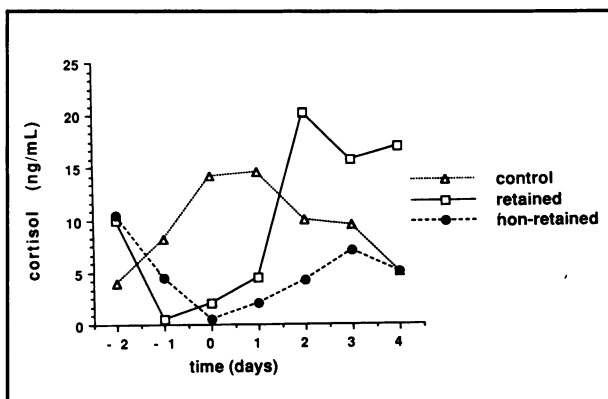


Figure 2. Mean peripheral concentrations of cortisol in cows retaining or not retaining the placenta after induced parturition or after spontaneous parturition. Calving occurred on day 0.

Discussion

Our results demonstrated that a combination of CP and Dex was highly efficacious in the induction of parturition in the cow, showing a significantly shorter time interval from treatment to parturition compared with the use of Dex alone ($p < 0.05$). This has been shown in at least two other studies (20,49), and demonstrates the efficacy of this approach in controlling the timing of parturition.

The incidence of retained placenta in both experiments was similar and was high for all induction treatments. In a recent review, Bretzlaff (50) reported on unpublished work which also showed no reduction in the incidence of retained placenta in beef cows treated with PGF within one hour after calving induced with Dex or PGF. In contrast to these findings, Gross *et al* (40) reported a markedly reduced incidence of retained placenta in dairy cows induced to calve with Dex and treated with DI within one hour of parturition. The reasons for the differences between these studies are not known. Studies involving the monitoring of PGF metabolite (PGM) concentrations in peripheral plasma showed that PGM was high at the time of parturition after Dex treatment (5) and was significantly higher in those cows which subsequently retained their placenta (42). Therefore, it is difficult to rationalize the use of PGF at calving to reduce placental retention.

In experiment 1, the first service conception rates and pregnancy rates in cows with placental retention were not significantly lower than in cows without placental retention. However, in experiment 2, both first service conception rates and pregnancy rates were significantly lower in cows that retained their placenta. Previous workers have similarly reported both significant and nonsignificant decreases in conception rates and pregnancy rates in beef cows with placental retention (7,27,51). In two reports, in which dairy cows were induced to calve, there was no significant reduction in either conception rate or pregnancy rate (7,52).

Cows with retained placentas and which received antibiotics had no improvement in fertility over untreated cows with retained placentas. This might have been expected since antibiotic treatment, while

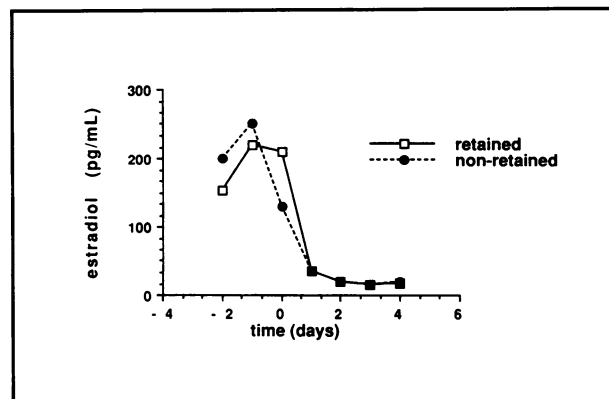


Figure 3. Mean peripheral concentrations of estradiol in cows retaining or not retaining the placenta after induction of parturition with cloprostenol and dexamethasone in combination, or with dexamethasone alone. Calving occurred on day 0.

alleviating systemic illness, did not affect the duration of placental retention.

Plasma progesterone levels showed a similar pattern of prepartal decline in all groups. The results of our study agree with previous reports of progesterone levels in normal parturient cows (2,15,42). We found no differences in plasma progesterone levels between cows with or without placental retention. This is in agreement with one study in which normally calving cows, with and without retained placentas, had similar prepartal levels of progesterone (53). However, in another study in which cows calved spontaneously, those that had retained their placenta had higher average prepartal progesterone than those without retained fetal membranes (54).

The relationship between increased peripheral cortisol concentrations and spontaneous parturition in noninduced (control) cows (Figure 2), agrees with results reported previously (2,55). However, in contrast to the sharp peak at parturition in our study, Adams and Wagner (55) observed that peripheral cortisol concentrations peaked by day 4 prepartum. The low cortisol levels at parturition in cows induced to calve with Dex (Figure 2) have been reported previously (32,55), and these authors suggested that exogenous glucocorticoids at dosages sufficient to elicit parturition in the cow can be expected to cause an absolute drop in endogenous plasma cortisol for 48 to 72 hours. The depression of endogenous cortisol through some feedback mechanism was evident in our study, although considerable individual variation occurred in cows at parturition. The increase in maternal peripheral cortisol concentrations in cows with retained fetal membranes has also been reported (47). The peripartur increase of serum cortisol in cows with retained placentas may be attributed to a stress response associated with inflammatory conditions in the endometrium or perhaps in response to increased PGF production associated with inflammation.

Serum estradiol concentrations increased rapidly prior to parturition in cows with and without placental retention. In cows without placental retention,

estradiol concentrations began to decrease markedly 24 h prior to parturition. This finding has been reported previously for normally calving cows (2,56). In cows with placental retention, estradiol levels remained elevated until the time of calving before dropping sharply. This phenomenon has also been reported previously in cows that had a high incidence of placental retention due to induction of parturition with dexamethasone (9). There is evidence that placental maturation near parturition in cows results in a decline in placental progesterone production and an increase in estrogen production (3,57). The maintenance of high estrogen levels until the time of calving may reflect the degree of placental maturation at the time of parturition (9).

In summary, calf viability, dystocia scores, and onset of lactation were similar in all groups. Cows receiving CP + Dex calved earlier and with less variability than cows induced with Dex alone. The results obtained in these two experiments show that administration of PGF within one hour postpartum is ineffective in reducing placental retention and do not agree with the original results of Gross *et al* (40).

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St. John's, Newfoundland July/juillet 5-8, 1992

Research Rostrum Monday, July 6, 1992

The Rostrum is intended to be a forum for dissemination of new information from research and for communication between researchers and clinicians. This announcement is a call for the submission of abstracts. A registration by speakers is not required for participation in the Rostrum.

The submission and selection of abstracts shall be as follows:

1. Abstracts must be clearly typed and submitted in the format as described below.
2. The original and one copy of the abstract should be sent (not by fax) to:
 Dr. Owen Slocombe
 Department of Pathology
 Ontario Veterinary College
 University of Guelph
 Guelph, ON
 N1G 2W1
 Tele: 519-823-8800 Ext 4652
 Fax: 519-824-5930
3. The telephone and fax numbers for the first author listed in the abstract should be included in a covering letter.
4. The deadline for receipt of abstracts (in Dr. Slocombe's office) is Thursday, April 30, 1992.
5. All abstracts received by the deadline and in the prescribed format will be published in the "Proceedings of the CVMA Convention" and in the "Rostrum Abstracts" under either "Oral Presentation" or "By Title".
6. The first 24 submissions received in the prescribed format will be assigned to "Oral Presentation" and given a 15 minute time slot in the program for presentation on July 6, 1992.
7. Abstracts not included for oral presentation will be under the heading "By Title".
8. The first author of each submission will be informed in early May on the status of the submission and will be sent a copy of the Rostrum Abstracts.

Please type the abstract on ordinary white bond paper (21.5 × 28 cm; 8.5 × 11 in.) leaving a 4 cm or 1.5 in margin on all sides. High quality printing is required as your abstract will be the "camera-ready" copy for reproduction. Dot matrix printing is unacceptable.

Type title with only the first letter and those of proper nouns in upper case; all other letters in lower case. Underline the title.

Author's name(s) on a new line in upper and lower case. Add an asterisk (*) after the name of the author making the presentation.

Affiliation and complete address on a new line and in upper and lower case. If more than one author, place the last name of the author in brackets after the appropriate address.

Skip two lines and type the body of the abstract which should not exceed more than 150 words. The abstract should state the purpose(s) of the study or investigation, basic procedures (selection of study subjects or experimental animals, and observational and analytic methods), main findings (give specific data and their statistical significance, if possible) and the principal conclusions. Symbols and signs (e.g. π) which must be hand lettered should be printed clearly in black ink.

Last date for receipt of the abstracts is Thursday, April 30, 1992.