CONTROL OF SEXUAL ACTIVITY IN RANCH COWS
BY INTRAMUSCULAR AND INTRAVAGINAL
ADMINISTRATION OF PROGESTAGENS

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Summary. Two trials were conducted to examine the effect of three progestagens, chlormadinone acetate (CAP), melengestrol acetate (MGA) and megestrol acetate (MA) on the sexual activity of ranch cows.

In the first trial, injection of CAP (6 mg/day) inhibited manifestation of oestrus in ten out of ten cows, while six of these cows showed full heat 4 to 6 days after cessation of treatment. When CAP was administered by intravaginal tampon (200 mg CAP/tampon), eight out of ten cows showed full heat during the 18 days of treatment, while two out of ten cows showed full heat in the 7 days immediately after cessation of treatment.

In the second trial, CAP was injected at 6 mg/day for 16 days and at 12 mg every alternate day for 16 days. MA or MGA was administered by intramuscular injection at 4 mg/day or 0.5 mg/day respectively or by intravaginal tampon at 100 mg/tampon or 60 mg/tampon respectively. With the exception of one cow (MA), all progestagens completely inhibited manifestation of oestrus when injected. When the progestagen was administered by tampon, two out of ten cows receiving MGA and two out of ten cows receiving MA showed oestrus during treatment. During the period 5 to 10 days after cessation of treatment, heat was shown by 100%, 80%, 70% and 70% of cows which received injections of CAP daily, CAP on alternate days, MGA or MA, respectively. The high incidence of anovulatory heats (20 to 80%) indicated that the first heat after cessation of progestagen treatment would be associated with low fertility.

INTRODUCTION

The efficiency of inhibition and synchronization of oestrus consequent upon the administration of a pharmaceutical substance, depends upon the chemical composition of the substance, its mode of administration, dosage and the endocrinological status of the individual animal. In the large animal field to date,

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most pharmaceutical substances have had progestational activity. In recent attempts to synchronize oestrus in cows, the progestagen has been injected intramuscularly (Wiltbank, Zimmerman, Ingalls & Rowden, 1965), intravenously (Zimbelman & Smith, 1966a) or included in the feed (Takeuchi, Shimizu & Toyoda, 1966; Zimbelman & Smith, 1966b). Apart from many inherent disadvantages, oral administration is not practicable on ranches in Central Africa. In ewes, progestagens have been administered by use of several methods, including an intra-vaginal tampon (Robinson, 1965; Curl, Cockrell, Bogard & Hudson, 1966; Foord, 1966). Little information is available about this mode of administration in cattle.

In the present studies, three progestagens were administered to typical Zambian ranch cows. Mode of administration was by injection (i.m.) or by intravaginal insertion of a tampon impregnated with the progestagen.

**MATERIALS AND METHODS**

Cows of indigenous breeds (live-weight 250 to 350 kg) were taken from the main herd maintained at this laboratory. The sexual and ovarian activity of these cows had been recorded for the previous 30 months. For convenience in handling, the cows were kept in groups of thirty to thirty-five animals.

The following progestagens were used: chlormadinone acetate (6-chloro-\(\Delta^6\)-dehydro-17\(\alpha\)-acetoxyprogesterone) (CAP), Imperial Chemical Industries; meclengestrol acetate (6\(\alpha\)-methyl-16 methylene-17-acetoxyprogesterone) (MGA), British Drug Houses; megestrol acetate (17\(\alpha\)-acetoxy-6-methyl progna 4:6-diene-3:20-dione) (MA), British Drug Houses.

Methods to detect oestrus, anovulatory oestrus and changes in gross morphology of the ovaries have been described (Symington & Hale, 1967). Ovaries were palpated per rectum at weekly intervals.

**Intramuscular injection**

The progestagen was suspended in arachis oil to give a concentration such that the daily dose for each cow was contained in 1 ml of oil. Injection was into the gluteal muscle.

**Intravaginal administration**

The requisite amount of progestagen for each cow was dissolved in 50 ml of chloroform, the solution applied to the tampon and the chloroform allowed to evaporate before the tampon was inserted into the vagina.

**Polyurethane foam.** Foams of varying density were used in the manufacture of tampons. In general, the denser the foam, the better was the retention of the tampon in the vagina. To aid removal of the tampon, a large button was attached to the anterior end of the tampon by passage of nylon thread through the tampon. When the tampon was positioned correctly in the vagina, its anterior end was in contact with the cervix and the looped end of thread was about 2 to 3 cm inside the exterior vulvae.

**Size of tampon.** Cylindrical tampons of varying size were tested. Satisfactory
retention was obtained with tampons of 10 cm diameter and 10 cm length. In the present trials, all tampons were of this size.

Insertion of tampon. Tampons were inserted using a polythene tube (40 cm long, 38 mm internal diameter). In order to minimize bacterial infection and to facilitate insertion of the tampon into the tube, tampons were coated with an antibiotic cream (Terramycin, Pfizer) immediately before insertion. Tampons were extruded from the tube into the anterior vagina by a plunger.

In both trials, administration of the progestagen began irrespective of stage in the oestrous cycle.

Experimental procedure
Two main trials were conducted. In Trial I, three groups, each of ten cows, were subjected to the following treatments:

Group I Control: Cows injected with arachis oil only.
Group II CAP in arachis oil injected i.m.
Group III CAP administered intravaginally on tampon.

Dose levels of CAP in this trial were 6 mg each day for 18 days by injection and 200 mg for intravaginal application.

In the second trial, seventy-one cows were used. With the exception of the control group which consisted of eleven cows, all groups contained ten cows. These groups were:

Group I Control group.
Group II CAP injected daily (6 mg each day).
Group III CAP injected on alternate days (12 mg per injection).
Group IV MGA injected daily (0.5 mg each day).
Group V MA injected daily (4 mg each day).
Group VI MGA administered intravaginally (60 mg per tampon).
Group VII MA administered intravaginally (100 mg per tampon).

All three progestagens, irrespective of route of application, were administered for 16 days.

RESULTS

Trial I
Before the administration of CAP, apparently functional corpora lutea were palpable in the ovaries of twenty-two cows. Subsequent changes in the gross morphology of the ovaries of the other eight cows indicated that the ovaries of these cows were also functional at the start of the trial.

During the period of injections, only one (cow 150) of the ten cows in Group II showed any sexual activity or ovulated (Table 1). It is of note that this cow showed silent heat only 2 days after injections had started. However, injected CAP did not suppress ovarian function completely since changes were detected in the ovarian gross morphology of most cows in this group, indicating follicular growth.

Four to 6 days after the final injection, six cows in Group II showed full
heat, one cow silent heat and one cow anovulatory heat. Cow 150 showed full heat 12 days after injections ended.

Three (out of ten) tampons were ejected prematurely—all shortly after palpation of ovaries on Day 11. During palpation of the ovaries, cows with tampons exhibited marked lordosis and strained to eject the tampons. Undoubtedly, the premature ejection of tampons was largely the result of palpation of the ovaries. In Group III, both cows which showed full heat in the 7 days following treatment (Table 1) had ejected their tampons prematurely. Further, one of these cows had shown full, the other silent heat during the 18 days of treatment. In both instances, the duration of the period between these activities was of normal cycle length (16 to 26 days). One cow ovulated the day after the tampon was removed. The oestrous cycle was of normal length in cows which retained their tampons until Day 18. This was substantive evidence that intravaginal administration of CAP did not synchronize oestrus.

**Trial 2**

At the start of the trial, fifty-six of the seventy cows had apparently functional corpora lutea. The ovaries of the remaining fourteen cows appeared to be functional but had no palpable corpora lutea.

During the period of administration, no cow which was injected with CAP or MGA showed oestrus or ovulated (Table 1). One of the ten cows injected with MA had an anovulatory heat on Day 15 of treatment. Irrespective of the progestagen used, corpora lutea which were present at the start of injections appeared to follow a normal pattern of development and regression during administration of the progestagen. In cows where palpable corpora lutea were

### Table 1

**Sexual Activity During and Subsequent to the Administration of Progestagens**

<table>
<thead>
<tr>
<th>Trial No.</th>
<th>Group No.</th>
<th>Treatment</th>
<th>No.</th>
<th>During treatment</th>
<th>5th to 10th day after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Full heat</td>
<td>Silent heat</td>
</tr>
<tr>
<td>I</td>
<td>I</td>
<td>Control</td>
<td>10</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>CAP injected daily</td>
<td>10</td>
<td>0</td>
<td>1*</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>CAP tampon</td>
<td>10</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>II</td>
<td>I</td>
<td>Control</td>
<td>11</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Injection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>CAP daily</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>CAP alternate days</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>MGA daily</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>V</td>
<td>MA daily</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>VI</td>
<td>MGA</td>
<td>10</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>VII</td>
<td>MA</td>
<td>10</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

* Cow no. 150.
absent at start of treatment, injection of a progestagen did not appear to affect the sporadic occurrence of follicles such as happens during the normal ovarian cycle (Symington & Hale, 1967).

Two cows in each tampon group showed full heat and three other cows experienced either silent or anovulatory heat during the 16 days of treatment. These levels of sexual and ovarian activity were considerably less than the level of activity shown by cows of the control group (Table 1). One tampon impregnated with MGA and five tampons impregnated with MA were ejected shortly after palpation of the ovaries.

The main feature of note regarding the degree of synchronization of oestrus achieved by the various treatments was the large number of anovulatory heats recorded between the 5th and 10th days after cessation of treatment (Table 1). As a proportion of total sexual and ovarian activity, the incidence of anovulatory heat varied between 20% and 80%. The manifestation of sexual and/or ovarian activity was also very irregular. With the exception of cows injected with CAP, cows in all other treatment groups showed recurrent sexual and/or ovarian activity at very short time intervals. For example, three cows to which MGA was administered intravaginally showed various combinations of full, silent and anovulatory heat in the 10 days following treatment. By contrast, three other cows in this group showed no activity whatsoever during this period. Indeed, two of these cows remained inactive for a further 2 weeks, i.e. until some 24 days after the end of treatment.

The various treatments had different effects on the length of the oestrous cycle at different stages of the trial. Throughout the trial, control cows exhibited a total of twenty-eight oestrous cycles. All cycles were of normal duration (16 to 26 days). During administration of MGA by tampon and MA by either route, six animals showed heat. Cycle length varied between 4 and 23 days. No cow receiving MGA by injection or CAP showed a complete cycle during this period. Immediately after treatment, six cows (four receiving MGA) showed oestrus twice within a few days (mean 5-2 days). Thereafter, cycle length returned to normal and irrespective of the progestagen used, mean length of the cycle was 18-6 (twenty-two cycles).

An observation of interest was that on removal, tampons impregnated with MGA had no smell and little adherent mucus. Tampons impregnated with MA had an offensive smell and a fair amount of adherent mucus. In the previous trial, tampons impregnated with CAP were covered with a copious amount of foul-smelling mucus.

DISCUSSION

The ultimate value of a progestagen can be determined only from its effect on the overall, long-term fertility of the recipient. Nevertheless, an immediate and partial evaluation is possible from the ability of the progestagen to affect the sexual and/or ovarian activity of the recipient in a manner which leads to a very high incidence of fertile oestrus in the few days subsequent to the cessation of treatment. With progestagens, such short-term evaluation implies the degree of inhibition of sexual and/or ovarian activity during administration of the
progestagen and the degree of synchronized, normal oestrus in the few days following administration of the progestagen.

Combination of information from the tabulated data shows that, out of a total of fifty cows to which a progestagen was given by injection, only one cow ovulated and one cow experienced an anovulatory heat during the period of administration of the progestagen (Table 1). In other words, satisfactory inhibition of oestrus was achieved by intramuscular injection of CAP, MGA or MA. By contrast, out of twenty-one control cows maintained in identical environmental circumstances, fifteen showed full heat and two showed silent heat during the same period.

Unfortunately, in the present studies, less success was achieved in synchronization than in inhibition of oestrus. When CAP was injected into thirty cows, (Trials 1 and 2) seventeen (57%) of these cows showed full heat between the 4th and 8th days after the end of treatment. Analogous figures for MGA and MA were 20% and 40% respectively. Strictly comparative data are not available from the literature. When CAP was fed to 236 cows under feed-lot conditions (Hansel, Donaldson, Wagner & Brunner, 1966), oestrus occurred in 87% of the cows between the 3rd and 7th days after feeding had ended. However, conception rate from service at this oestrus was only 50%. At a daily injection rate of 0.4 mg of MGA, Zimbelman & Smith (1966a) inhibited ovulation and oestrus in eight out of eight heifers during administration of the progestagen. However, no information was given about the subsequent synchronization of oestrus and ovulation. When these workers administered MGA orally (Zimbelman & Smith, 1966b), a high degree of synchronization of oestrus was obtained but conception rate was only 42%. The results of Zimbelman & Smith, the present results and other findings (Wiltbank et al., 1965; Ray, Emmerson & Melampy, 1961) confirm that the major weakness in this technique at present is the low fertility subsequent to the withdrawal of the progestagen. In our studies, palpation of the ovaries showed a high incidence of anovulatory oestrus which would cause low fertility. That this endocrinological dysfunction was directly attributable to the administration of the progestagen was indicated by the concomitant absence of anovulatory oestrus in control cows and by the generally very low level of anovulatory oestrus (1.7%) exhibited by other cows at this laboratory (Symington & Hale, unpublished results). The possibility that administration of progesterone rather than a progestagen may be more effective in this respect, is suggested by the findings of Lamond, Little & Holmes (1964) that 99 out of 100 cows ovulated within 24 hr of manifestation of oestrus. However, the possibility that other endocrinological dysfunction also occurs after administration of a progestagen was indicated by the subsequent manifestation of oestrus at very frequent and irregular intervals. This observation may well be associated with the findings of Zimbelman & Smith (1966b) that prolonged administration of MGA causes pronounced follicular and oestrogenic activities.

The failure of progestagens to inhibit and to synchronize oestrus when applied intravaginally could be ascribed to two causes: the premature ejection of tampons and/or the absorption of progestagens from the tampons at non-physiological rates. In the present studies between 10% and 50% of tampons
Inhibition and synchronization of oestrus in cows

were ejected prematurely. However, even in cows in which tampons remained in situ, progestagens did not inhibit oestrus effectively. The vaginal discharge which was noted after removal of tampons might have influenced absorption of progestagens applied intravaginally and thus the ability of progestagens to inhibit and to synchronize oestrus when applied by this route. In this respect, it is pertinent that the amount of vaginal discharge appeared to vary with either the amount or the type of progestagen applied to the tampon. Thus 60 mg MGA applied intravaginally resulted in a small amount of vaginal discharge whereas 200 mg CAP applied by the same procedure resulted in a copious amount of foul-smelling mucus in the vagina. Unfortunately, bacteriological studies could not be conducted to examine the effect of type and amount of progestagen on the bacterial population of the vagina. Accordingly, it is not certain whether the inability of progestagens to inhibit oestrus was due to a loss of progestagens from the vagina in the copious mucus, by an effect of bacteria, or by an inherent unsuitability of this route of administration in cattle which would contrast with its suitability in sheep (Robinson, 1965).

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REFERENCES


