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# Use of Melengestrol Acetate-Based Treatments to Induce and Synchronize Estrus in Seasonally Anestrous Ewes<sup>1,2,3</sup>

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**ABSTRACT:** Ten experiments utilizing 1,659 ewes were conducted to determine the potential of melengestrol acetate (MGA)-based treatments in inducing and synchronizing estrous activity in ewes during the nonbreeding season. In May or June, ewes were given .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup> or control diet and(or) a subsequent i.m. injection of zeranol, estradiol-17 $\beta$ , or oil vehicle. Fertile rams were introduced, and estrous and(or) lambing responses were determined. In Exp. 1, more ( $P < .01$ ) ewes given MGA for 14 d followed by 5 mg of zeranol (i.m.) were in estrus than controls. Melengestrol acetate and zeranol independently induced estrus in Exp. 2, with MGA-treated ewes exhibiting the greatest lambing response ( $P < .05$ ). The optimum duration of feeding MGA was 8 d vs 11 or 14 d (Exp. 3). In Exp. 4, as the dose of zeranol increased, synchrony of estrus increased but lambing response decreased. A dose of 1.25 mg of zeranol

represented a compromise in estrous and lambing response and was determined to be optimally effective when given 54 h after the last feeding of MGA (Exp. 5). Shortcomings in lambing responses were treated in Exp. 6 by supplementing ewes with MGA after breeding, which proved unsuccessful, and in Exp. 7 by substituting estradiol-17 $\beta$  for zeranol, which proved effective when given 54 h after the last feeding of MGA (Exp. 8). In Exp. 9, use of MGA + estradiol increased ( $P < .05$ ) the estrous and subsequent lambing response of 30-d postpartum ewes temporarily weaned of their lambs. In contrast, lambing response of 90-d postpartum ewes treated with MGA + estradiol was not increased by temporary removal of lambs (Exp. 10). These data collectively support the hypothesis that treatment of ewes with MGA + estradiol is an effective and practical approach for inducing and synchronizing a fertile estrus in ewes during the non-breeding season.

Key Words: Sheep, Melengestrol, Estrous Synchronization, Zeranol, Estradiol, Lamb Removal

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## Introduction

To increase producer profitability in the livestock industry, animal production efficiency must increase. In the sheep industry, efficiency of production can be characterized by the number of lambs weaned per ewe per year. Currently, the national average number of

lambs weaned per ewe per year is approximately one (CRIS, 1993). Two approaches to increase the numbers of lambs produced per ewe per year are to increase lambing frequency and(or) to increase the lambing rate. Accelerated lambing programs such as the Cornell Star System are management strategies that have had some success in increasing production efficiency (Hogue and Magee, 1987). Efficiency of accelerated programs is compromised by the increased management demands distributed throughout the year and the low genetic propensity of ewes to produce out of season. Unfortunately, current production strategies do not take full advantage of the relatively short gestation period of ewes and therefore do not capitalize on the potential ability of ewes to produce two lamb crops in one year.

Since the 1960s, methods have been available to induce and synchronize estrus in seasonally anestrous ewes (Evans et al., 1962; Southcott et al., 1962; Bindon and Roberts, 1964).

Melengestrol acetate (MGA) is a commercially available synthetic progestogen that was first used in

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<sup>3</sup>Mention of a trade name or proprietary product does not constitute a guarantee by the University of Missouri and does not imply its approval to the exclusion of other products that may also be suitable.

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feedlot heifers to suppress estrus and improve feed efficiency and rate of gain (Bloss et al., 1966; O'Brien et al., 1968). Melengestrol acetate is unique in that it is orally active in ruminants, and, compared with other orally active progestogens, MGA is the most potent (Zimbelman, 1963). Melengestrol acetate is easily administered through the feed, economically appealing due to the small dose required, and effective at suppressing estrus.

The general objectives of these investigations were initially to evaluate the potential use of MGA-based treatments to induce and synchronize estrous activity in seasonally anestrous ewes. Subsequently, efforts were devoted to optimizing treatment protocols and finally assessing the use of those treatments in postpartum- and(or) suckling-induced anestrous ewes. Ten experiments are presented with this general focus.

## Materials and Methods

### General

A series of 10 experiments was conducted from May 1987 to November 1995 to investigate the effect of MGA-based therapies on the induction and synchronization of estrus in anestrous ewes and their lambing performance. Hampshire, Columbia, Romanov, Rambouillet, and Rambouillet crossbred ewes ( $n = 1,659$ ) from the University of Missouri sheep facility were utilized. When two or more breeds were involved in a single study, the effect of breed was balanced across treatment groups. Treatment diets consisted of MGA (Carl Akee, Lewisburg, OH) mixed with crushed corn and fed so that ewes received .125 mg of MGA each morning and evening (the MGA diet) or an equivalent amount of the corn diet (the control diet) for the specified number of days. At specified times after the last treatment feeding, ewes received i.m. injections of specified doses of zeranol (Ralgro<sup>®</sup> Pitman-Moore, Terre Haute, IN), estradiol-17 $\beta$ , or a 1-mL i.m. injection of the corn oil vehicle. Immediately following the last treatment feeding, ewes were introduced to fertile, semen-tested rams that were fitted with brisket markers. Rams were managed in two groups, with each group being alternated in(out) of the ewe flock each morning and evening to expose ewes to rested rams every 12 h. At no time did ram:ewe ratios exceed 1:20. In studies in which estrus data were collected, ewes were checked for estrus every 12 h, and the occurrence of estrus was determined based on the presence of ewe-rump markings and(or) ewes standing to be mounted. In each experiment, unless stated otherwise, the variables assessed included the proportion of ewes exhibiting estrus, time of estrus, and(or) the proportion of ewes lambing, lambing date, and percentage of lambs born per ewe exposed and(or) lambing.

### *Experiment 1: Designing an Melengestrol Acetate-Based Therapy for Breeding Ewes Out of Season*

In designing a therapy to induce and synchronize breeding activity in anestrous ewes, we chose the compounds MGA and zeranol because of their progestational and estrogenic actions (respectively), cost effectiveness, simple application, availability from other livestock industries, and ease of administration.

*Hypothesis.* A greater proportion of ewes exposed to rams during the non-breeding season will exhibit estrus and subsequently lamb following treatment with MGA and zeranol than will those ewes receiving a control treatment.

*Approach.* In May 1987, 24 Hampshire ewes were divided into two groups. One group (MGA + zeranol,  $n = 12$ ) was fed the MGA diet for 14 d, and 30 h after the last treatment feeding ewes received an i.m. injection of 5 mg of zeranol. The remaining ewes (controls,  $n = 12$ ) contemporaneously received the control diet and an i.m. injection of oil. Rams were introduced immediately after the injections and remained with the ewes for 17 d, during which ewes were checked daily for estrus.

### *Experiment 2: Independent or Combined Effects of Melengestrol Acetate and Zeranol*

We concluded from the results of Exp. 1 that MGA + zeranol was potentially useful for inducing and synchronizing estrus in anestrous ewes. The contribution of each of the components, MGA and zeranol, to the estrous and lambing responses, however, was not known and thus was investigated in Exp. 2.

*Hypothesis.* Treatment of anestrous ewes with both MGA and zeranol results in a greater percentage of ewes exhibiting a synchronous estrus and lambing than treatment of ewes with MGA alone, zeranol alone, or a control treatment.

*Approach.* In May 1988, 43 Hampshire and 45 Rambouillet ewes were allotted to a  $2 \times 2$  factorial arrangement of treatments consisting of MGA or control diets and i.m. injections of zeranol or oil. As in Exp. 1, MGA + zeranol-treated ewes ( $n = 23$ ) received the MGA diet for 14 d, followed 30 h after the last treatment feeding with an i.m. injection of 5 mg of zeranol. The remaining ewes contemporaneously received the MGA treatment (i.e., MGA diet + oil injection,  $n = 20$ ), zeranol treatment (i.e., control diet + 5 mg zeranol injection,  $n = 22$ ), or control treatment (i.e., control diet + oil injection,  $n = 23$ ). Rams were introduced immediately following the injections and remained with the ewes for 21 d, during which time ewes were checked for estrus.

### *Experiment 3: Effect of Duration of Treatment with Melengestrol Acetate*

In an effort to maximize the induction and synchronization of estrus and the percentage of ewes

lambing following MGA-based treatments, we investigated the effect of the duration of feeding the MGA diet. No injections were given to ewes in Exp. 3.

*Hypothesis.* The proportion of ewes in estrus and lambing will vary in relation to the length of time (8, 11, or 14 d) the MGA diet is fed.

*Approach.* In May 1989, 67 Rambouillet ewes were divided into three groups that received MGA for 8 d ( $n = 20$ ), 11 d ( $n = 21$ ), or 14 d ( $n = 26$ ). Rams were introduced after the last treatment feeding and remained with the ewes for 21 d, during which time ewes were checked for estrus.

#### *Experiment 4: Effect of Dose of Zeranone Injected*

The conclusion drawn from the results of Exp. 3 was that 8 d of treating ewes with the MGA diet was sufficiently efficacious and the most economical. Consequently, in Exp. 4 and subsequent experiments, ewes were treated with MGA for 8 d. Focus was then given in Exp. 4 to determine the effect of the dose of zeranol on the proportion of ewes exhibiting an induced and synchronized estrus and the percentage of ewes lambing following the MGA + zeranol treatment.

*Hypothesis.* The proportion of ewes exhibiting estrus and lambing will vary relative to the dose (0, .3125, 1.25, or 5 mg) of zeranol injected 30 h after the last feeding of MGA.

*Approach.* In June 1990, a mixed population of 197 ewes were fed MGA for 8 d and then randomly assigned to receive 0, .3125, 1.25, or 5 mg of zeranol 30 h after the last feeding of MGA ( $n = 51, 48, 48,$  and  $50$ , respectively). Rams were introduced after the injections and remained with the ewes for 21 d. Ewes were checked for estrus for 21 d following ram introduction.

#### *Experiment 5: Effect of Time of Injection of Zeranone*

From the results of Exp. 4, we concluded that the greatest proportion of ewes exhibited a synchronous estrus and lambing when a dose of 1.25 mg of zeranol was injected 30 h after the last feeding of MGA. In Exp. 5, the importance of the time of injection of zeranol (relative to the last feeding of MGA) on the lambing responses of ewes was investigated.

*Hypothesis.* The lambing responses of ewes will vary relative to when injections of 1.25 mg of zeranol are given (30, 42, or 54 h) following the last feeding of MGA.

*Approach.* In June 1991, a mixed population of 253 ewes was fed MGA for 8 d and then randomly assigned to one of six groups that received either 1.25 mg of zeranol (**Z**) or oil (**O**) at 30 h (Z30,  $n = 64$ ; O30,  $n = 19$ ), 42 h (Z42,  $n = 63$ ; and O42,  $n = 20$ ), or 54 h (Z54,  $n = 64$ ; O54,  $n = 23$ ) after the last feeding of MGA. Rams were introduced after the injections and re-

mained with the ewes for 21 d. In this experiment, only the percentage of ewes lambing and the percentage of lambs born per ewe exposed and/or lambing were determined.

#### *Experiment 6: Effect of Supplemental Feeding of Melengestrol Acetate Following Treatments*

The disparity between the proportion of ewes in estrus and the proportion of ewes lambing (Exp. 4) prompted an investigation (Exp. 6) into the suggestion that supplemental exposure of early pregnant animals to progestogens would increase the proportion of animals that carry a pregnancy to term (Johnson et al., 1958).

*Hypothesis.* Treatment of ewes with the MGA diet for 9 d, beginning 12 d after ram introduction, will increase the proportion of ewes lambing.

*Approach.* In May 1992, 220 Rambouillet ewes were fed MGA for 8 d; 54 h after the last feeding, fertile rams were introduced and remained with the ewes for 42 d. Ewes were randomized to receive as follows: no further treatment (MGA;  $n = 113$ ), an injection of 1.25 mg of zeranol given 54 h after the last feeding of MGA (MGA + zeranol;  $n = 52$ ), or the MGA + zeranol treatment and an additional 9 d of the MGA diet beginning 12 d after the injection of zeranol (MGA + zeranol + MGA;  $n = 55$ ). The variables assessed consisted of percentage of ewes lambing and percentage of lambs born per ewe exposed and/or lambing.

#### *Experiment 7: Effect of Zeranone vs Estradiol-17 $\beta$ Following Melengestrol Acetate Treatment*

Observations gleaned from the results of Exp. 1 to 6 supported the hypothesis that MGA-based therapies were effective for inducing and synchronizing estrus in a significant proportion of anestrus ewes. Opportunities existed, however, to increase the proportion of ewes that exhibited estrus and subsequently lambing. The approach chosen to address this concern was to replace the injection of 1.25 mg of zeranol with an injection of an estrogen that is native to the ewe, at a dose previously proven in other applications (i.e., 20  $\mu$ g estradiol-17 $\beta$ ; Beck and Reeves, 1973).

*Hypothesis.* The proportion of ewes in estrus and lambing following treatment with MGA + estradiol-17 $\beta$  (20  $\mu$ g) is greater than that of ewes treated with MGA + zeranol (1.25 mg).

*Approach.* In June 1992, 63 crossbred Rambouillet ewes were fed MGA for 8 d; 54 h after the last feeding of MGA, ewes ( $n = 21$ /group) received an i.m. injection of either oil (MGA + oil), 1.25 mg of zeranol (MGA + zeranol), or 20  $\mu$ g of estradiol-17 $\beta$  (MGA + estradiol). Rams were introduced after the last feeding of MGA and remained with the ewes for 21 d. Ewes were checked for estrus for 72 h following ram introduction.

### *Experiment 8: Effect of Time of Injection of Estradiol-17 $\beta$*

The conclusion drawn from the results of Exp. 7 was that ewes administered 20  $\mu\text{g}$  of estradiol-17 $\beta$  following the last feeding of MGA performed comparably if not with slight superiority to ewes treated with 1.25 mg of zeranol, as assessed collectively by the proportion of ewes induced and(or) synchronized to mate and lamb. Unlike MGA + zeranol-treated ewes, ewes that received estradiol-17 $\beta$  exhibited a significant improvement in induction and synchronization of estrus and lambing rate beyond that of control ewes that received MGA + oil. In Exp. 8, the importance of the time of injection of 20  $\mu\text{g}$  of estradiol-17 $\beta$  (relative to the last feeding of MGA) to the estrous and lambing responses of ewes was investigated.

*Hypothesis.* The estrous and lambing responses of ewes will vary relative to when an injection of 20  $\mu\text{g}$  of estradiol-17 $\beta$  is given (36, 48, or 54 h) following the last feeding of MGA.

*Approach.* In May 1993, 131 Rambouillet and 60 Hampshire ewes were used. Ewes were fed MGA (n = 149) or the control diet (n = 42) for 8 d. Ewes treated with MGA were randomized between breeds to receive an i.m. injection of 20  $\mu\text{g}$  of estradiol-17 $\beta$  (E) or oil (O), 36 h (E36, n = 37; O36, n = 13), 48 h (E48, n = 38; O48, n = 12), or 54 h (E54, n = 37; O54, n = 12) after the last feeding of MGA. Ewes that were fed the control diet received no injections. Rams were introduced after the last treatment feeding and remained with the ewes for 13 d, during which time ewes were checked for estrus.

### *Experiment 9: Lamb Removal vs Melengestrol Acetate + Lamb Removal + Estradiol-17 $\beta$*

From the results of Exp. 8, we concluded that treatment of ewes for 8 d with MGA and then an injection of 20  $\mu\text{g}$  of estradiol-17 $\beta$  54 h after the last feeding of MGA was the most efficacious. In contrast to Exp. 1 through 8, in which the MGA-based therapy was developed for use in seasonally anestrous ewes, Exp. 9 and 10 tested the utility of the MGA-based therapy to induce and synchronize estrus in seasonally anestrous ewes that were also suckling lambs. The suckling stimulus is a potent inhibitor of the reproductive processes (McNeilly, 1988), and temporary removal of offspring can be an effective means of inducing the resumption of reproductive activity (Williams, 1990). Therefore, in Exp. 9 and 10 the use of MGA-based therapies, combined with temporary lamb removal, was investigated as a means to enhance reproductive efficiency in postpartum ewes nursing lambs during the anestrous season.

*Hypothesis.* The proportion of lactating ewes exhibiting estrus during the anestrous season and subsequently lambing in response to temporary lamb removal can be enhanced with the use of MGA-based therapies.

*Approach.* In May 1995, a mixed population of 161 ewes that were suckling lambs was randomly assigned on d 30 postpartum to receive MGA or control diets for 8 d. Immediately following the last treatment feeding, lambs were removed from all ewes. Lambs were returned to all ewes 54 h later, and MGA-treated ewes were given an i.m. injection of 20  $\mu\text{g}$  of estradiol-17 $\beta$  (MGA + Lamb Removal + Estradiol; n = 82), control ewes were given an i.m. injection of oil (Lamb Removal; n = 79). Both groups of ewes were balanced for effects of breed of ewe and number of lambs suckled. Rams were introduced after the last treatment feeding and remained with the ewes for 7 d, during which time ewes were checked for estrus.

### *Experiment 10: Melengestrol Acetate + Estradiol vs Melengestrol Acetate + Lamb Removal + Estradiol*

An effort was made to determine the effect of temporary lamb removal on subsequent lambing response of 90-d postpartum ewes that were nursing lambs and treated with MGA + estradiol-17 $\beta$ .

*Hypothesis.* The lambing response of postpartum ewes treated with MGA + estradiol-17 $\beta$  is greater in ewes temporarily weaned of their lambs during the interval from last feeding of MGA to injection of estradiol-17 $\beta$  (i.e., for 54 h).

*Approach.* In June 1995, 395 90-d postpartum Rambouillet ewes that were nursing lambs were fed MGA for 8 d. Immediately after the last feeding of MGA, lambs were removed from 205 ewes and returned 54 h later, at which time ewes received an i.m. injection of 20  $\mu\text{g}$  of estradiol-17 $\beta$  (MGA + Lamb Removal + Estradiol). The remaining 190 ewes contemporaneously received MGA + estradiol, and lambs were not removed. Rams were introduced to ewes after the last feeding of MGA and remained with the ewes for 24 d.

### *Statistics*

Proportion of ewes in which estrus was induced and synchronized, proportion of ewes lambing per ewe exposed, and the percentage of lambs born per ewe exposed were analyzed using a standard normal distribution where  $Z \geq 1.96$  was significant at the  $P < .05$  level. Differences between proportions were tested by dividing the difference by its standard error (Snedecor and Cochran, 1989) and comparing to a Z distribution. The proportion of lambs born per ewe lambing was analyzed using chi-square test in which  $\chi^2 \geq 3.84$  was significant at the  $P < .05$  level.

## **Results**

### *Experiment 1*

All MGA + zeranol-treated ewes (12/12) were in estrus within 36 h after injection of zeranol. In

Table 1. Induction and synchronization of estrus and subsequent lambing responses of ewes treated with melengestrol acetate (MGA) and/or zeranol<sup>a</sup>

Variable	Treatment group			
	Control <sup>b,c</sup> (n = 23)	Zeranol <sup>b,d</sup> (n = 22)	MGA <sup>e,c</sup> (n = 20)	MGA + Zeranol <sup>e,d</sup> (n = 23)
Estrous response (Cumulative % of exposed ewes in estrus relative to time of injection-ram introduction)				
24 h	4.3 ± 4.3 <sup>f</sup>	9.1 ± 6.1 <sup>f</sup>	15.0 ± 8.0 <sup>f</sup>	95.7 ± 4.3 <sup>g</sup>
36 h	4.3 ± 4.3 <sup>f</sup>	36.4 ± 10.3 <sup>g</sup>	35.0 ± 10.7 <sup>g</sup>	95.7 ± 4.3 <sup>h</sup>
60 h	8.7 ± 5.9 <sup>f</sup>	40.9 ± 10.5 <sup>g</sup>	60.0 ± 11.0 <sup>g</sup>	95.7 ± 4.3 <sup>h</sup>
84 h	13.0 ± 7.0 <sup>f</sup>	54.5 ± 10.6 <sup>g</sup>	80.0 ± 8.9 <sup>gh</sup>	95.7 ± 4.3 <sup>h</sup>
21 d	30.4 ± 9.6 <sup>f</sup>	68.2 ± 9.9 <sup>g</sup>	90.0 ± 6.7 <sup>gh</sup>	100.0 ± 1.4 <sup>h</sup>
Lambing responses				
Ewes lambing/ewe exposed	30.4 ± 9.6 <sup>f</sup>	31.8 ± 9.9 <sup>f</sup>	75.0 ± 9.7 <sup>g</sup>	43.5 ± 10.3 <sup>f</sup>
Lambs born/ewe exposed	47.8 ± 10.4 <sup>f</sup>	36.4 ± 10.3 <sup>f</sup>	100.0 ± 2.2 <sup>g</sup>	47.8 ± 10.4 <sup>f</sup>
Lambs born/ewe lambing	157.1	114.3	133.3	110.0

<sup>a</sup>Ewes were treated in May 1988 and allowed to mate with fertile rams for 21 d after treatment. Values are means ± SE %.

<sup>b</sup>Ewes were fed the control diet (which lacked MGA) for 14 d.

<sup>c</sup>Ewes received a 1-mL i.m. injection of oil 30 h after the last treatment feeding.

<sup>d</sup>Ewes received a 5-mg i.m. injection of zeranol suspended in oil 30 h after the last treatment feeding.

<sup>e</sup>Ewes were fed .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 14 d.

<sup>f,g,h</sup>Numbers within rows with no superscripts in common differ ( $P < .05$ ).

contrast, ewes that received the control diet and an injection of oil failed to exhibit estrus within the 17-d interval following treatment (0/12;  $P < .01$ ). More ewes lambed per ewe exposed in the MGA + zeranol group than the control group (6/12 vs 0/12, respectively;  $P < .01$ ). Percentages of lambs born per ewe exposed and lambs born per ewe lambing were greater in the MGA + zeranol group than in the control group (58% and 117% vs 0% and 0%, respectively;  $P < .01$ ).

### Experiment 2

In testing the independent or combined effects of MGA and zeranol, the combined effect of MGA and zeranol resulted in the greatest proportion of ewes in estrus within 24, 36, and 60 h of injections (Table 1). Independently, treatment of ewes with MGA alone or zeranol alone was able to induce estrus in a significant proportion of ewes by 36 h after injection; however,

that response was significantly less than the estrous response associated with MGA + zeranol. By 84 h and 21 d after injections, the proportion of ewes in estrus that received MGA + zeranol or MGA alone did not differ. Subsequent to estrus, the proportion of ewes lambing and lambs born per ewe exposed to rams was greatest among ewes that received only MGA (75% and 100%, respectively;  $P < .05$ ). Treatment of ewes with zeranol (i.e., MGA + zeranol and zeranol alone) either was not advantageous (control vs zeranol,  $P > .10$ ) or reduced the lambing responses (MGA vs MGA + zeranol,  $P < .05$ ).

### Experiment 3

The duration of feeding MGA (.25 mg MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 8, 11, or 14 d) did not affect the estrous response, proportion of ewes lambing per ewe exposed, or lambs born per ewe lambing ( $P > .05$ , Table 2). In contrast, across all treatments, the

Table 2. Induction and synchronization of estrus and subsequent lambing responses of ewes treated with melengestrol acetate (MGA) for 8, 11, or 14 days<sup>a</sup>

Variable	Duration of MGA treatment <sup>b</sup>		
	8 d (n = 20)	11 d (n = 21)	14 d (n = 26)
Estrous responses ( $\bar{x} \pm SE$ %)			
Ewes in estrus/ewe exposed	90.0 ± 6.7	71.4 ± 10.0	92.3 ± 5.2
Lambing responses ( $\bar{x} \pm SE$ %)			
Ewes lambing/ewe exposed	65.0 ± 10.7	61.9 ± 10.6	57.7 ± 9.7
Lambs born/ewe exposed	95.0 ± 4.9 <sup>c</sup>	85.7 ± 7.6 <sup>cd</sup>	73.1 ± 8.7 <sup>d</sup>
Lambs born/ewe lambing	146.2	138.5	126.7

<sup>a</sup>Ewes were treated in May 1989 and allowed to mate with fertile rams for 21 d after treatment.

<sup>b</sup>Ewes were fed .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup>.

<sup>c,d</sup>Numbers within rows with no superscripts in common differ ( $P < .05$ ).

Table 3. Estrus and lambing responses ( $\bar{x} \pm SE$  %) of ewes treated with melengestrol acetate (MGA) and 0, .3125, 1.25 or 5 mg of zeranol<sup>a,b</sup>

Variable	0 mg (n = 51)	.3125 mg (n = 48)	1.25 mg (n = 48)	5 mg (n = 50)
Ewes exposed in estrus within				
48 h Following ram introduction	21.6 ± 5.8 <sup>c</sup>	33.3 ± 6.8 <sup>c</sup>	70.8 ± 6.6 <sup>d</sup>	94.0 ± 3.4 <sup>e</sup>
4 d Following ram introduction	60.8 ± 6.8 <sup>c</sup>	54.2 ± 7.2 <sup>c</sup>	81.3 ± 5.6 <sup>d</sup>	96.0 ± 2.8 <sup>e</sup>
21 d Following ram introduction	74.5 ± 6.1 <sup>c</sup>	70.8 ± 6.7 <sup>c</sup>	83.3 ± 5.4 <sup>c</sup>	96.0 ± 2.8 <sup>d</sup>
Ewes lambing/ewe exposed	47.1 ± 7.0 <sup>c</sup>	39.6 ± 7.1 <sup>cd</sup>	29.2 ± 6.6 <sup>cd</sup>	12.0 ± 4.6 <sup>d</sup>
Lambs born/ewe exposed	74.5 ± 6.1 <sup>c</sup>	64.6 ± 6.9 <sup>cd</sup>	37.5 ± 7.0 <sup>d</sup>	14.0 ± 4.9 <sup>d</sup>
Lambs born/ewe lambing	158.3	163.2	128.6	116.7

<sup>a</sup>Ewes were treated in June 1990 and allowed to mate with fertile rams for 21 d after treatment.

<sup>b</sup>Ewes were fed .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 8 d and given zeranol suspended in corn oil or 1 mL of oil 30 h after the last feeding of MGA.

<sup>c,d,e</sup>Numbers within rows with no superscripts in common differ ( $P < .05$ ).

greatest number of lambs were born to ewes exposed to MGA for 8 d vs 14 d ( $P < .05$ ), with ewes treated for 11 d producing an intermediate response. Consequently, these observations, as well as economic and management considerations, dictated the conclusion that treatment of ewes with .25 mg MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 8 d was the most effective treatment.

#### Experiment 4

The proportion of ewes exhibiting estrus within 48 h, 4 d and 21 d after injection was greatest for ewes receiving the 5 mg dose of zeranol ( $P < .05$ , Table 3). In contrast, the 5-mg dose was least desirable when assessed in terms of the percentage of ewes lambing per ewe exposed to the ram ( $P < .05$ ). Collectively, the 1.25-mg dose of zeranol represented a compromise in efforts to achieve both an acceptable estrous synchronization response and associated lambing response. In summary, as the dose of zeranol injected increased, an inverse relationship occurred between the estrous response and the lambing response.

#### Experiment 5

Time of injection of zeranol did not affect the percentage of ewes lambing per ewe exposed during a 21-d breeding season when compared with ewes that

received MGA + oil (Table 4). On the basis of previous observations (Exp. 1, 2, and 4), however, efforts to not only induce estrus but also to synchronize estrus dictated the use of an estrogenic compound. When zeranol was injected 30 h after the last feeding of MGA, fewer lambs were born per ewe exposed than for ewes treated at 54 h. Consequently, while a 42-h or 54-h injection was equally effective, the decision was made to give injections 54 h after the last feeding of MGA in subsequent studies.

#### Experiment 6

Supplemental exposure of ewes to MGA following breeding did not affect the percentage of ewes lambing per ewe exposed to rams when compared with MGA-treated or MGA + zeranol-treated ewes ( $P > .05$ , Table 5). In contrast, more ewes lambed per ewe exposed to rams in the MGA + zeranol group than the MGA alone group ( $P < .05$ ). Furthermore, a greater percentage of lambs was born per ewe exposed to rams in the MGA + zeranol group than the MGA or MGA + zeranol + MGA groups ( $P < .05$ ).

#### Experiment 7

A greater proportion of ewes treated with MGA + estradiol was in estrus by 24, 48, and 72 h following

Table 4. Lambing responses ( $\bar{x} \pm SE$  %) of ewes following treatment with zeranol or oil given 30, 42, or 54 h after the last feeding of melengestrol acetate (MGA)<sup>a,b</sup>

Variable	Treatment group			
	Oil <sup>c</sup> (n = 62)	30 h (n = 64)	42 h (n = 63)	54 h (n = 64)
Ewes lambing/ewe exposed	37.1 ± 6.1	40.6 ± 6.1	49.2 ± 6.3	43.8 ± 6.2
Lambs born/ewe exposed	53.2 ± 6.3 <sup>d</sup>	53.1 ± 6.2 <sup>d</sup>	65.1 ± 6.0 <sup>de</sup>	68.8 ± 5.8 <sup>e</sup>
Lambs born/ewe lambing	143.5	130.8	132.3	157.1

<sup>a</sup>Ewes were treated in June 1991 and allowed to mate with fertile rams for 21 d after treatment.

<sup>b</sup>Ewes were fed .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 8 d and given a 1.25-mg i.m. injection of zeranol or oil at the specified time after the last feeding of MGA.

<sup>c</sup>Pooled data from ewes receiving oil at 30, 42 and 54 h after the last feeding of MGA.

<sup>d,e</sup>Numbers within rows with no superscripts in common differ ( $P < .07$ ).

Table 5. Lambing responses ( $\bar{x} \pm SE$  %) of ewes treated with melengestrol acetate (MGA), MGA + zeranol, or MGA + zeranol followed by a supplemental feeding of MGA for 9 d beginning 12 d after ram introduction<sup>a</sup>

Variable	Treatment group		
	MGA <sup>b</sup> (n = 113)	MGA + Zeranol <sup>bc</sup> (n = 52)	MGA + Zeranol + MGA <sup>bcd</sup> (n = 55)
Ewes lambing/ewe exposed	46.9 ± 4.7 <sup>e</sup>	67.3 ± 6.5 <sup>f</sup>	56.4 ± 6.7 <sup>ef</sup>
Lambs born/ewe exposed	72.6 ± 4.2 <sup>e</sup>	100.0 ± 1.9 <sup>f</sup>	80.0 ± 5.4 <sup>e</sup>
Lambs born/ewe lambing	154.8	148.6	141.8

<sup>a</sup>Ewes were treated in May 1992 and allowed to mate with rams for 42 d after treatment.

<sup>b</sup>Ewes were fed .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 8 d.

<sup>c</sup>Ewes received a 1.25-mg i.m. injection of zeranol 54 h following last feeding of MGA.

<sup>d</sup>Twelve days after the injection of zeranol-ram introduction, ewes were fed .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 9 d.

<sup>e,f</sup>Numbers within rows with no superscripts in common differ ( $P < .05$ ).

injections than ewes that received MGA + oil ( $P < .01$ ; Table 6). Estrous response of ewes to MGA + zeranol was comparable to that of the MGA + estradiol treated-ewes at 24 h after injection and intermediate to the responses of MGA + oil-treated and MGA + estradiol-treated ewes at 48 and 72 h after injections. At lambing, a tendency existed for more MGA + estradiol-treated ewes to lamb per ewe exposed to rams than MGA + oil-treated ewes (38% vs 14%,  $P = .066$ ). Percentage of lambs born per ewe exposed was greater for ewes receiving MGA + estradiol than for ewes receiving MGA + oil (42.7% vs 14.0%, respectively,  $P < .05$ ), with the MGA + zeranol treatment producing an intermediate response (24.0%). Collectively, the slight advantage of MGA + estradiol-treated ewes to exhibit a synchronous estrus and respond by producing a greater percentage of lambs per ewe exposed, in conjunction with the native aspect of estradiol-17 $\beta$ , prompted the focus of further studies on the MGA + estradiol treatment.

### Experiment 8

A greater proportion of MGA- than non-MGA-treated ewes exhibited estrus during the 13-d mating

interval following the last treatment feeding ( $P < .01$ , Table 7). When injections of estradiol-17 $\beta$  were given 54 h after the last feeding of MGA, a greater proportion of ewes were in estrus than when injections were given at 36 h ( $P < .06$ ) or 48 h ( $P < .01$ ) after the last feeding. At lambing, a greater proportion of MGA-treated than non-MGA-treated ewes lambled and produced more lambs per ewe exposed ( $P < .01$ ). No differences existed across treatment groups in proportion of lambs born per ewe lambing. Based on these estrous and lambing response data, treatment of ewes with MGA, followed 54 h after the last treatment feeding with 20  $\mu$ g of estradiol-17 $\beta$ , collectively produced the most efficacious response.

### Experiment 9

The estrous response of spring-lambing, 30-d postpartum, lactating ewes to temporary removal of their lambs for 54 h was significantly improved by superimposing the MGA + estradiol-17 $\beta$  treatment identified as most efficacious in Exp. 8 (i.e., MGA + lamb removal + estradiol,  $P < .05$ , Table 8). At lambing, the positive response from the combined approach

Table 6. Induction and synchronization of estrus and subsequent lambing responses ( $\bar{x} \pm SE$  %) of ewes treated with melengestrol acetate (MGA) followed by an i.m. injection of zeranol, estradiol-17 $\beta$ , or oil<sup>ab</sup>

Variable	Treatment group		
	MGA + Oil (n = 21)	MGA + Zeranol (n = 21)	MGA + Estradiol (n = 21)
Percentage of exposed ewes in estrus relative to the time of injection			
24 h	19.0 ± 8.6 <sup>c</sup>	52.0 ± 10.9 <sup>d</sup>	61.9 ± 10.6 <sup>d</sup>
48 h	43.0 ± 10.8 <sup>c</sup>	67.0 ± 10.3 <sup>cd</sup>	86.0 ± 7.6 <sup>d</sup>
72 h	52.0 ± 10.9 <sup>c</sup>	67.0 ± 10.3 <sup>cd</sup>	86.0 ± 7.6 <sup>d</sup>
Ewes lambing/ewe exposed <sup>e</sup>	14.0 ± 7.6	24.0 ± 9.3	38.0 ± 10.6
Lambs born/ewe exposed	14.0 ± 7.6 <sup>c</sup>	24.0 ± 9.3 <sup>cd</sup>	42.7 ± 10.8 <sup>d</sup>
Lambs born/ewe lambing	100.0	100.0	112.5

<sup>a</sup>Ewes were treated in June 1992 and allowed to mate with fertile rams for 21 d after treatment.

<sup>b</sup>Ewes were fed .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 8 d and received a 1-mL i.m. injection of oil, 1.25 mg of zeranol or 20  $\mu$ g of estradiol-17 $\beta$  54 h after the last feeding of MGA.

<sup>c,d</sup>Numbers within rows with no superscripts in common differ ( $P < .05$ ).

<sup>e</sup>Effect of MGA + oil vs MGA + estradiol ( $P = .066$ ).

Table 7. Lambing responses ( $\bar{x} \pm SE$  %) of ewes following treatment with melengestrol acetate (MGA) and estradiol-17 $\beta$  or oil given 36, 48 or 54 h after the last feeding of MGA<sup>a</sup>

Variable	Treatment group				
	Control <sup>b</sup> (n = 42)	MGA + Oil <sup>c</sup> (n = 37)	Estradiol 36 h <sup>c</sup> (n = 37)	Estradiol 48 h <sup>c</sup> (n = 38)	Estradiol 54 h <sup>c</sup> (n = 37)
Ewes in estrus/ewe exposed					
within 54 h of ram introduction <sup>g</sup>	2.4 $\pm$ 2.4 <sup>d</sup>	56.8 $\pm$ 8.1 <sup>ef</sup>	54.1 $\pm$ 8.2 <sup>e</sup>	50.0 $\pm$ 8.1 <sup>e</sup>	75.7 $\pm$ 7.1 <sup>f</sup>
within 13 d of ram introduction	21.4 $\pm$ 6.3 <sup>d</sup>	70.3 $\pm$ 7.5 <sup>ef</sup>	64.9 $\pm$ 7.9 <sup>e</sup>	52.6 $\pm$ 8.1 <sup>e</sup>	83.8 $\pm$ 6.1 <sup>f</sup>
Ewes lambing/ewe exposed	4.8 $\pm$ 3.3 <sup>d</sup>	45.9 $\pm$ 8.2 <sup>e</sup>	40.5 $\pm$ 8.1 <sup>e</sup>	34.2 $\pm$ 7.7 <sup>e</sup>	48.6 $\pm$ 8.2 <sup>e</sup>
Lambs born/ewe exposed	9.5 $\pm$ 4.5 <sup>d</sup>	64.9 $\pm$ 7.9 <sup>e</sup>	56.8 $\pm$ 8.1 <sup>e</sup>	57.9 $\pm$ 8.0 <sup>e</sup>	75.7 $\pm$ 7.1 <sup>e</sup>
Lambs born/ewe lambing	200.0	141.2	140.0	169.2	155.6

<sup>a</sup>Ewes were treated in May 1993 and allowed to mate with fertile rams for 13 d after treatment.

<sup>b</sup>Ewes were fed the control diet (which lacked MGA) for 8 d.

<sup>c</sup>Ewes were fed .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 8 d and given a 1-mL i.m. injection of oil or 20  $\mu$ g of estradiol-17 $\beta$  30, 42, or 54 h after the last feeding of MGA.

<sup>d,e</sup>Numbers within rows with no superscripts in common differ ( $P < .06$ ).

<sup>g</sup>Effect of estradiol 54 h vs MGA + oil ( $P = .078$ ).

persisted, with not only a greater proportion of ewes lambing and lambs born per ewe exposed but also more lambs born per ewe lambing ( $P < .05$ ).

### Experiment 10

The lambing response of 90-d postpartum ewes treated with MGA + estradiol-17 $\beta$  was not improved by temporarily removing their lambs during the interval from last feeding of MGA to injection of estradiol-17 $\beta$  ( $P > .47$ , Table 9).

## Discussion

The number of lambs weaned per ewe per year is the principal determinant of producer profitability in the sheep industry. One approach to increase the number of lambs weaned per ewe per year is to increase lambing frequency. Unfortunately, seasonal constraints on breeding activity of ewes limit this

approach. On foreign markets, progestin-based therapies (e.g., PRID, Ainsworth and Wolynetz, 1982; CIDR, Greyling and Brink, 1987) are available to induce and synchronize estrous activity in ewes out of season. In the United States, no products are marketed for reproductive management of sheep; however, such products are available in the cattle, swine, and equine industries. The focus of this series of studies was to design a therapy that was economical, easily administered and effective at inducing and synchronizing breeding activity in ewes out-of-season, using compounds that are available to U.S. producers in the other livestock industries. The approach was to mimic the progesterone and estrogen profiles of cycling ewes in noncycling ewes. Melengestrol acetate, an orally active synthetic progestin, and zeranol, a nonsteroidal estrogen, satisfied these criteria and were initially selected for evaluation in these experiments.

In Exp. 1, treatment of ewes for 14 d with MGA followed 30 h later by an i.m. injection of zeranol

Table 8. Estrus and lambing responses ( $\bar{x} \pm SE$  %) of 30-d postpartum ewes that were nursing lambs to short-term lamb removal or melengestrol acetate (MGA) + estradiol-17 $\beta$  and short-term lamb removal<sup>a</sup>

Variable	Treatment group	
	Lamb removal <sup>b</sup> (n = 79)	MGA + lamb removal + estradiol <sup>c</sup> (n = 82)
Ewes in estrus/ewe exposed	13.9 $\pm$ 3.9 <sup>d</sup>	29.3 $\pm$ 5.0 <sup>e</sup>
Ewes lambing/ewe exposed	1.3 $\pm$ 1.3 <sup>d</sup>	18.3 $\pm$ 4.3 <sup>e</sup>
Lambs born/ewe exposed	1.3 $\pm$ 1.3 <sup>d</sup>	31.7 $\pm$ 5.14 <sup>e</sup>
Lambs born/ewe lambing	100.0 <sup>d</sup>	173.3 <sup>e</sup>

<sup>a</sup>Ewes were treated in May 1995 and allowed to mate with fertile rams for 7 d after treatment.

<sup>b</sup>Ewes were fed the control diet (which lacked MGA) for 8 d, and lambs were removed following the last feeding of MGA. Lambs were returned 54 h later and ewes received a 1-mL i.m. injection of oil.

<sup>c</sup>Ewes were fed .25 mg of MGA·ewe<sup>-1</sup>·d<sup>-1</sup> for 8 d, and lambs were removed immediately following the last feeding of MGA.

<sup>d,e</sup>Numbers within rows with no superscripts in common differ ( $P < .05$ ).

resulted in a significant portion of ewes exhibiting a synchronous estrus and lambing. Efforts in Exp. 2 to dissect the contribution of the individual components of the MGA + zeranol therapy used in Exp. 1 revealed that both MGA and zeranol independently were capable of inducing estrus, but lacked the efficacy of the combined approach in generating a synchronous estrous response. Lambing response of ewes treated with zeranol (i.e., MGA + zeranol and zeranol alone), however, was significantly inferior to the lambing response of ewes that received only MGA. Later studies (Exp. 8 and 9) supported the observation from Exp. 2 that pretreatment of ewes during the nonbreeding season (May or June) with MGA, prior to ram introduction, increased the proportion of ewes in estrus and lambing beyond that of ewes not treated with MGA. The reason the MGA pretreatment provoked the expression of estrus has not been determined. Perhaps MGA 1) facilitated ovarian production of estrogen during treatment (Garcia-Winder et al., 1987), thus promoting the expression of estrus once MGA was removed; 2) increased the responsiveness of behavioral centers in the brain to estrogen, thus facilitating the ability of endogenous levels of estrogen to induce estrous behavior (Anderson et al., unpublished data); or 3) acted through a combination of the two approaches, or alternative mechanisms. Nonetheless, the observation that anestrous animals treated with progestins exhibited estrus upon withdrawal was not unique, because other investigators have reported similar responses (Umberger and Lewis, 1992; Safranski et al., 1992; Jabbar et al., 1994).

From a management perspective, support could be given for the use of MGA alone in a natural mating system in which a synchronous estrus could be disastrous if ram numbers or quality was inadequate. A concern with the use of progestins, especially their long-term use, has been their effect on subsequent fertility. Hansel (1967) and Roche (1974) reported that cows synchronized with long-term progestin treatments (18 to 21 d) had lower first service conception and fertility rates than cows either un-

treated or treated with a short-term progestin. In those studies, conception rates subsequent to the synchronized estrus were not different from that predicted for untreated controls. In seasonally anestrous ewes, unlike in cows, fertility at the induced estrus is of paramount importance because frequently anestrous ewes will not have a second mating opportunity before returning to the anestrous condition. The concern over the fertility of the induced estrus prompted an investigation in Exp. 3 into the effect of duration of feeding MGA for 8, 11, or 14 d on estrous and lambing response. The conclusion was that, although no difference existed among 8, 11 or 14 d of MGA treatment in the proportion of ewes in estrus during the 21-d breeding season, the proportion of lambs born per ewe exposed to the ram declined as the duration of MGA treatment increased. Consequently, for these and economic reasons, all future treatments with MGA were limited to 8 d. Efforts to further resolve the effect of a shorter duration exposure to MGA were not made.

The unfortunate shortcoming associated with using only MGA was the poor estrous synchronization response it provided compared with the use of MGA + zeranol. This shortcoming was viewed as a considerable limitation to the future use of an MGA-based therapy to facilitate the adoption of sheep artificial insemination programs. In an effort to achieve both a synchronous estrus and a high lambing response to treatments, we pursued several approaches, utilizing both MGA and zeranol. These approaches consisted of the following: 1) determining a minimally effective dose of zeranol (Exp. 4), 2) determining an effective time of injection of zeranol (Exp. 5), and 3) supplementing ewes after breeding with additional MGA as a way to minimize losses associated with ewes that conceive but fail to maintain pregnancy (Exp. 6). In these studies we determined that an injection of 1.25 mg of zeranol produced a compromise in estrous and lambing responses (Exp. 4) and was most effective when given 54 h after the last feeding of MGA (Exp. 5). In Exp. 6, efforts to minimize early embryonic losses by supplementing ewes after breeding with MGA

Table 9. Effect of short-term lamb removal on lambing response ( $\bar{x} \pm SE$  %) of 90-d postpartum ewes, that were nursing lambs and treated with melengestrol acetate (MGA) + estradiol-17 $\beta$ <sup>a</sup>

Variable	Treatment group <sup>b</sup>	
	MGA + estradiol <sup>c</sup> (n = 190)	MGA + lamb removal + estradiol <sup>cd</sup> (n = 205)
Ewes lambing/ewe exposed	38.4 $\pm$ 3.5	40.0 $\pm$ 3.4
Lambs born/ewe exposed	50.5 $\pm$ 3.5	54.1 $\pm$ 3.5
Lambs born/ewe lambing	135.4	131.5

<sup>a</sup>Ewes were treated in June 1995 and allowed to mate with fertile rams for 24 d after treatment.

<sup>b</sup>No significant difference was found between treatment groups ( $P > .47$ ).

<sup>c</sup>Ewes were fed .25 mg of MGA-ewe<sup>-1</sup>·d<sup>-1</sup> for 8 d, and 54 h after the last feeding of MGA ewes were injected i.m. with 20  $\mu$ g of estradiol-17 $\beta$ .

<sup>d</sup>Lambs were removed following the last feeding of MGA and returned 54 h later.

were unsuccessful. The unrealized opportunity this approach could have delivered was a second synchronized estrus among ewes that failed to conceive following injection of zeranol.

A final approach taken to optimize the estrous and lambing responses was to substitute the injection of zeranol with an injection of estradiol-17 $\beta$  (Exp. 7). Estradiol-17 $\beta$  was equally effective, if not superior to zeranol, at inducing and synchronizing estrus and improving lambing performance when given 54 h after the last feeding of MGA (Exp. 7 and 8). Unlike results for MGA + zeranol-treated ewes, estrous and lambing response of MGA + estradiol-treated ewes differed from results for ewes that received MGA + oil. Although the use of zeranol was appealing from a number of aspects, including availability, ease of use and cost, retrospectively the use of zeranol likely contributed to the suboptimum lambing responses in the previous studies. Estradiol-17 $\beta$  was chosen because it was native to ewes and is responsible for inducing estrus and the ovulatory process in cycling ewes (Beck and Reeves, 1973). The dose of estradiol-17 $\beta$  chosen (20  $\mu$ g) was 1/60th of the dose of zeranol (1.25 mg) on a mass basis and 1/20th of the dose of zeranol used based on a reported potency of zeranol being 30% that of estradiol-17 $\beta$  (Elsasser et al., 1983). In the study by Elsasser et al. (1983), ovariectomized ewes were given zeranol or estradiol-17 $\beta$ , and the characteristics of the surge of LH were determined. It was observed that both compounds evoked surges of LH that differed in a dose-response manner. In addition, as the dose of zeranol increased, the surge of LH occurred later in time relative to the time of injection. In contrast, the surges of LH evoked in response to increasing doses of estradiol-17 $\beta$  all occurred at approximately the same time. The consequence of this circumstance with the use of zeranol may have been that the time of estrus and insemination, which occurred soon after injection, became dissociated from the time of ovulation, which likely occurred much later in the zeranol-treated ewes, thus increasing the opportunity for fertilization failure to occur.

Alternatively, the magnitude of the dose of zeranol may have affected oviductal transport of ova. Hawk and Cooper (1974, 1975) reported that estrogen increased the direction of uterine contractions towards the oviducts, which promoted the movement of sperm toward the egg. When estrogen levels declined, uterine contractions were directed towards the cervix, promoting the movement of the fertilized egg into the uterus. The long half-life of zeranol (Malinckrodt Veterinary, Inc., personal communication) may have disrupted this process.

Finally, it was hypothesized that because zeranol has a long duration of action, it may have had a detrimental effect on development of the induced corpus luteum. In support of this hypothesis, Emons et al. (1984) reported that the delivery of estradiol-17 $\beta$  to ewes during the luteal phase suppressed the

secretion of LH, the principal luteotropin (Goodman, 1988).

In Exp. 9 and 10, the efficacy of the MGA + estradiol treatment (from Exp. 8) was tested in one of the more difficult groups of ewes in which to induce and synchronize estrus and maintain a pregnancy to term; i.e., 30 to 90-d lactating, postpartum anestrous ewes treated in May or June. It has been reported that suckling-offspring limit the dam's ability to return to reproductive competence. Schirar et al. (1989) reported that ewes suckling lambs had a longer postpartum interval to first estrus and a greater incidence of short luteal phases than non-suckled ewes (60% vs 7%, respectively). In cattle, early weaning at 30-d postpartum reduced the interval to first estrus and increased the number of cows conceiving (Smith and Vincent; 1972). Similarly, temporary calf removal, when used in conjunction with progestin treatments, increased the number of cows in estrus and the proportion pregnant following treatment (Smith et al., 1979; Kiser et al., 1980).

Removal of the suckling stimulus from cows causes an increase in pulsatile secretion of LH (Atterberry et al., 1988) and a greater LH responsiveness to LHRH (Smith et al., 1983). In Exp. 9, 13.9% of ewes in the lamb-removal-only group exhibited estrus, possibly due to an increase in LH-stimulated secretion of estradiol-17 $\beta$ . The disparity in the proportion of ewes in estrus and lambing in the lamb-removal-only group may have been attributed to a ram and(or) lamb removal-induced estrus in non-progestin primed ewes, thus predisposing the CL that formed in the lamb-removal-only group to function inadequately (Cognie et al., 1982; Martin et al., 1986). In contrast, the progestin-primed ewes may have been more predisposed to exhibit estrus and maintain a functional CL, which thus preserved pregnancy.

Finally, in Exp. 10, the inability to detect a difference in lambing response between MGA + lamb removal + estradiol ewes vs ewes treated with MGA + estradiol may indicate either the timing for lamb removal was inappropriate or the treatment was sufficiently powerful to recruit the preponderance of the responsive ewes.

## Implications

In the sheep industry, efficiency of production can be characterized by the number of lambs produced per ewe per year. One approach to increase the number of lambs produced per ewe per year is to increase lambing frequency; however, seasonal influences limit ewes' ability to lamb more than once per year. We suggest the data contained within this report support the premise that the melengestrol acetate-based therapies have a practical application as a means of inducing and synchronizing estrous in ewes during the non-breeding season. Consequently, this approach provides the opportunity to lamb ewes more than once per year.

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