# روش های نوین و اقتصادی در همزمان سازی فحلی و تخمک ریزی گوسفند و بز

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# Introduction

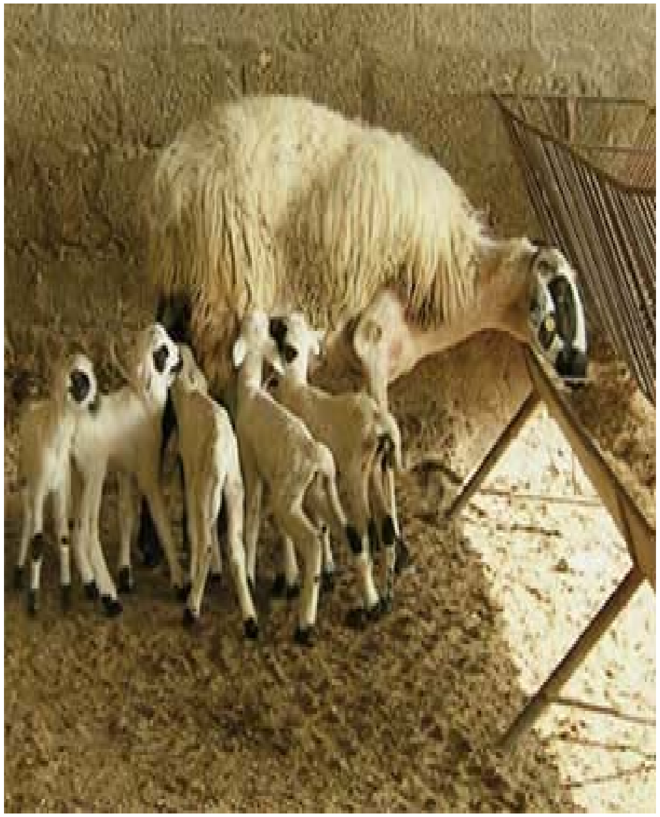
- Reproductive performance is one of the largest determining factors of profitability in today's sheep & goat industry.
- Synchronization of estrus is a key component in reproductive management of sheep and goat flocks.

ES **Advantages**;

- A shorter and more consistent lambing season
- Increased Lamb Uniformity
- Implementing Reproductive Technologies i.e. FTAI, MOET
- Out of Season Breeding & Lambing
- Higher Prolificacy rates??

ES **Disadvantages**;

- Costs and Labor
- Reduced Fertility?



# Reproductive Characteristics of Ewes and Does

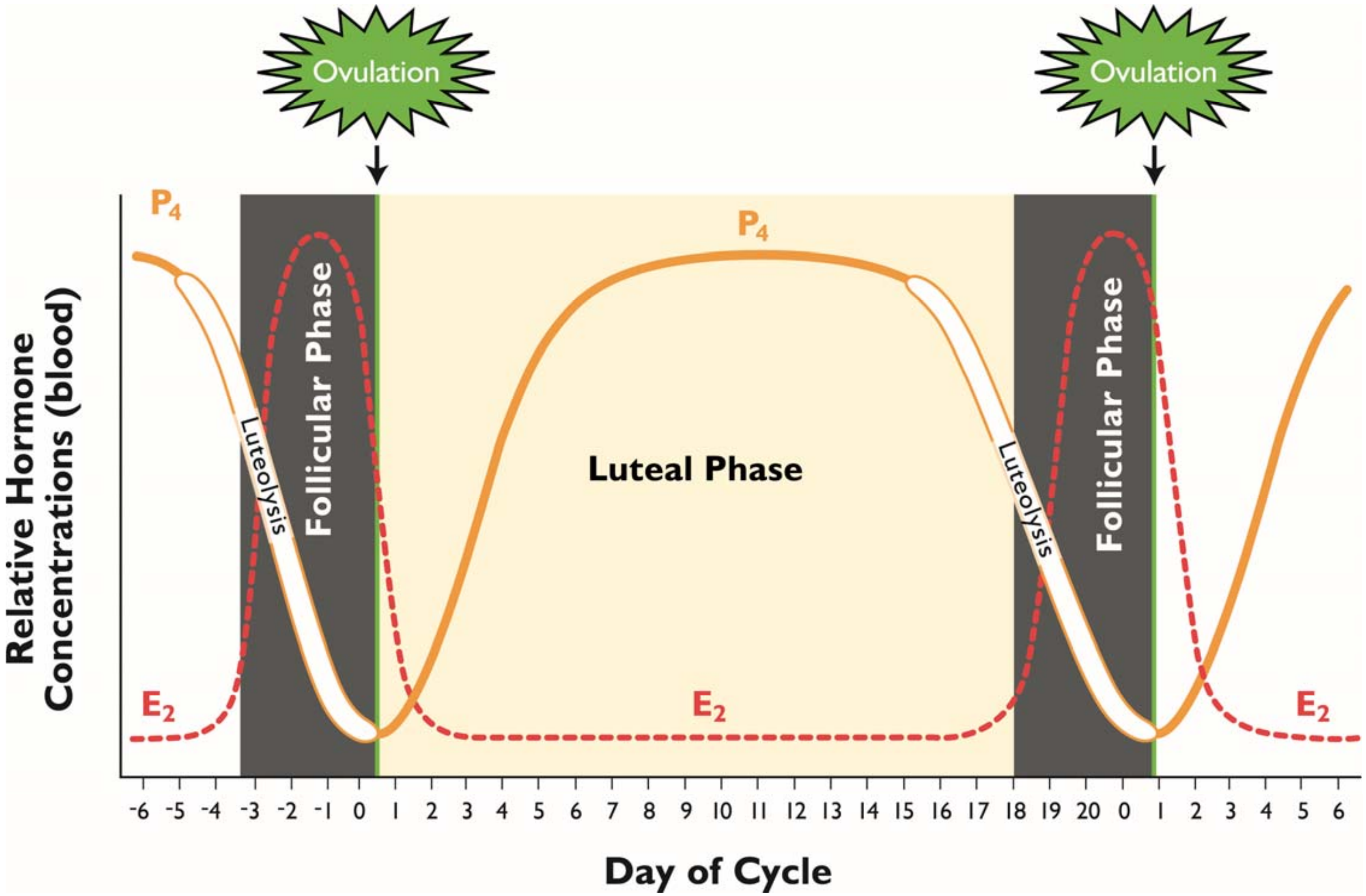
## SHEEP AND GOATS REPRODUCTION BASICS

| | Sheep | | Goats | |
|---|---|---|---|---|
| | Average | Range | Average | Range |
| Puberty | 5-12 months | | 6-8 months | 4-12 |
| Estrus cycle | 17 days | 14-19 days | 21 days | 18-24 days |
| Standing estrus | 30 hours | 15-45 hours | 36 hours | 24-48 hours |
| Ovulation (hours after estrus) | About 24 hours after onset | | 36 hours | 9-72 hours |
| Gestation | 148 days | 144-150 days | 150 days | 145-152 days |
| Ovulation rate | ~1.5 | 1-4 | ~1.7 | 1-4 |

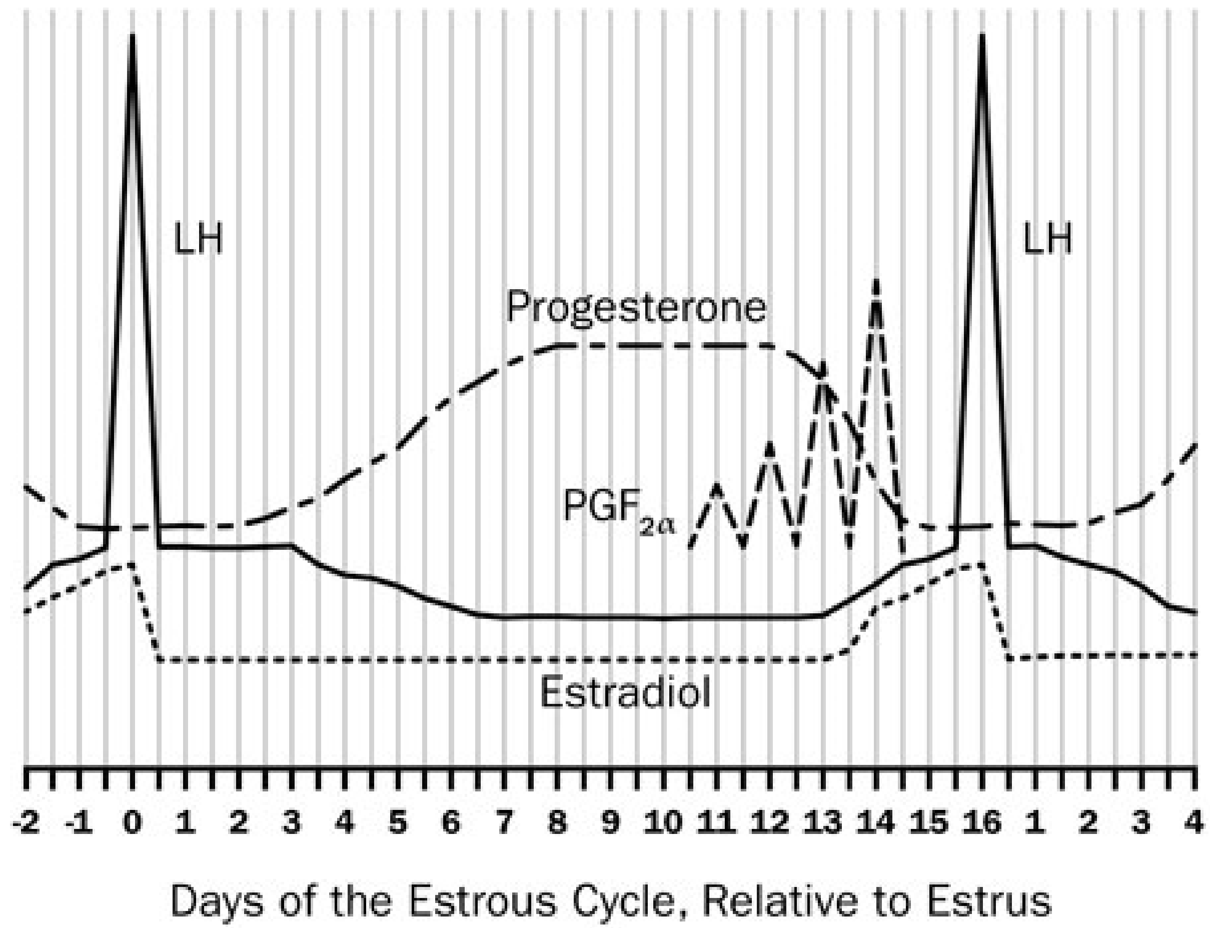
**Table 2.** Conception Rates by Age of Ewe and Month of Breeding

| Month of Breeding | Conception % | | | All Ages |
|---|---|---|---|---|
| | 1 year-old | 2year- old | 3 year-old | |
| August مرداد | 40.1 | 83.6 | 87.7 | 70.5 |
| October مهر | 66.6 | 93.1 | 94.3 | 84.7 |
| December آذر | 74.7 | 95.3 | 93.9 | 88.0 |
| **Overall** | **60.5** | **90.7** | **90.2** | |

# Ovarian Cycle in Goat



# Ovarian Cycle in Sheep




Sheep Production Handbook (2002). The average length of cycle used for sheep is 17 days. 90% of the cycles are 14-19 days long, with an average of about 17 days

# Reproductive Endocrinology in Sheep and Goat

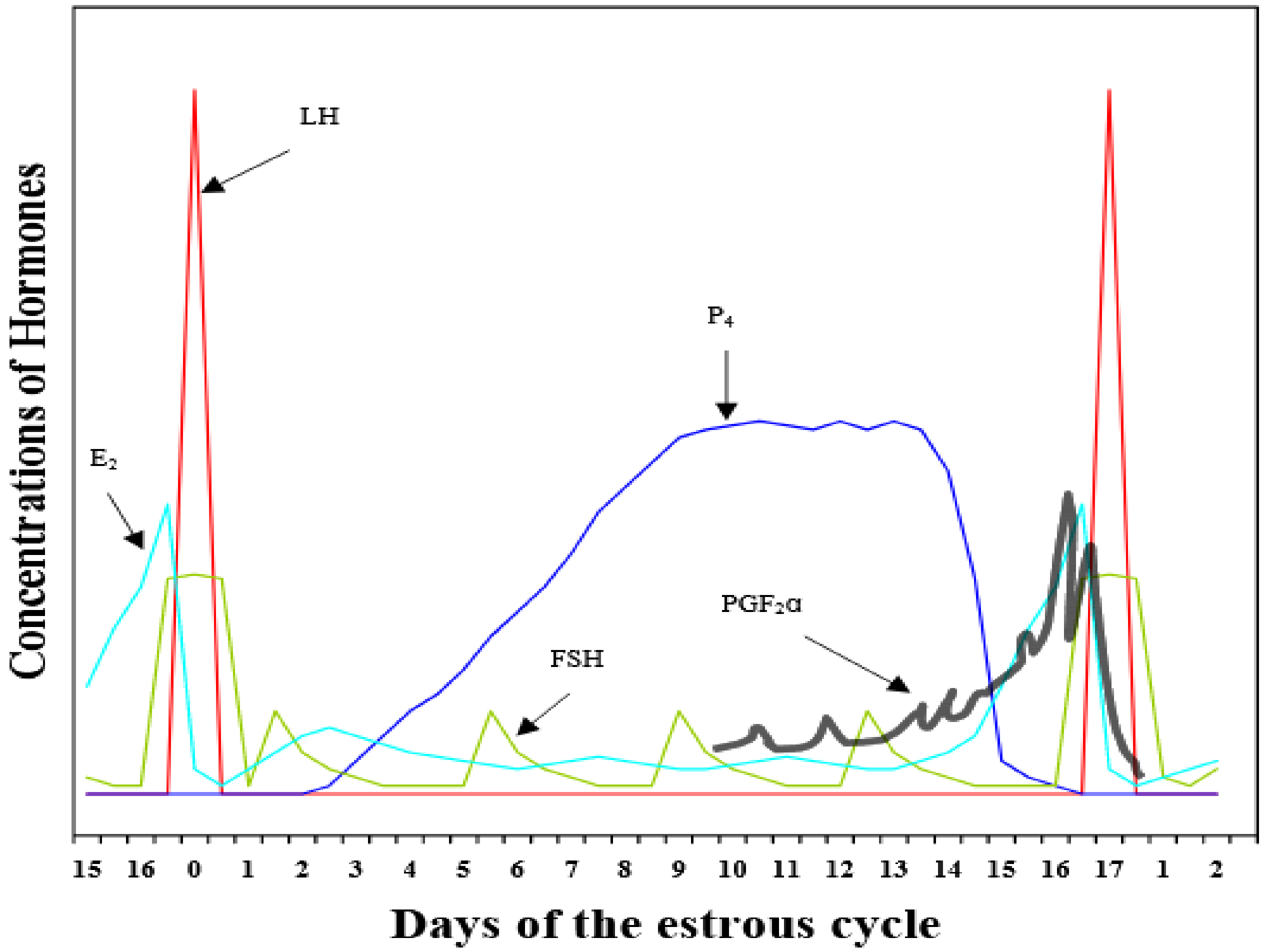
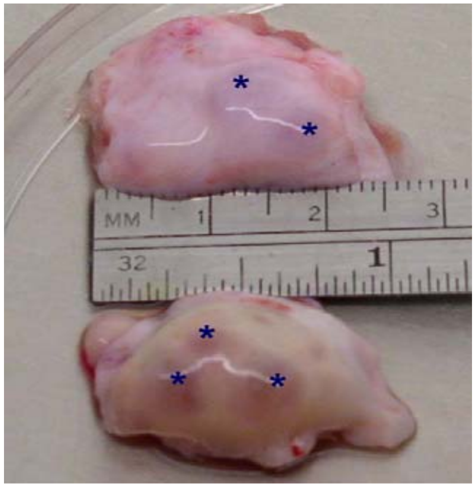
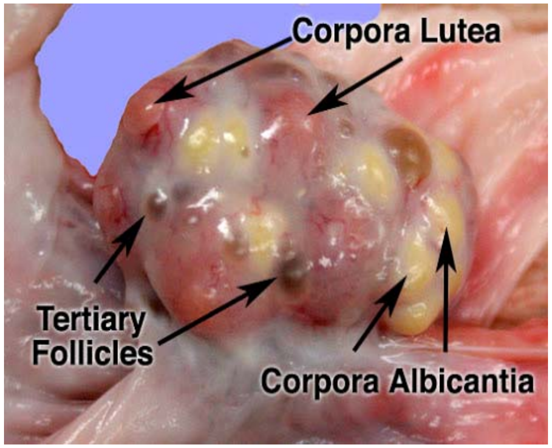



Figure 1. Patterns of concentrations of follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol-17β ($E_2$), progesterone ($P_4$), and prostaglandin $F_2\alpha$ in peripheral blood of the ewe during the estrous cycle.

ES in Sheep and Goat;

- Manipulation of either the luteal or the follicular phase of the estrous cycle.
- In does and ewes, the opportunity for control is greater during the luteal phase, which is of longer duration and more responsive to manipulation.
- Strategies can be employed to extend the luteal phase by supplying exogenous progesterone or to shorten this phase by prematurely regressing existing CL



# ES Methods

- Progestagens (oral progesterone, CIDR, Sponge, and Implants)
- $PGF_{2\alpha}$
- PMSG
- GnRH
- hCG
- Day/light regimens
- Melatonin implant
- Ram /Buck effect
- Estradiol

# Melengestrol Acetate (MGA) Feed Supplement

- Orally active, synthetic progestagen used for the suppression of estrus in feedlot heifers.
- It has also been used for the induction of a fertile estrus in **seasonally anovular ewes**.
- Feeding of a supplement (MGA 100 Premix™) containing MGA (0.25 mg of MGA/animal/day) once or twice daily for a duration of **8 to 12 d in non-breeding season** and for **14 d in breeding season**.
- Co-treatments of PMSG, PG-600 (PMSG/hCG), Zeranol
- **Rate of estrus out of season varies from 50% to 100%** .The pregnancy rate among treated ewes has been established at about **60% with a range of 30% to 85%.**
- 100 Premix™ which is sold for about $475.00 for 25 kg, the cost of treatment is $0.02/animal/day or $0.24/animal for the duration of the total treatment.

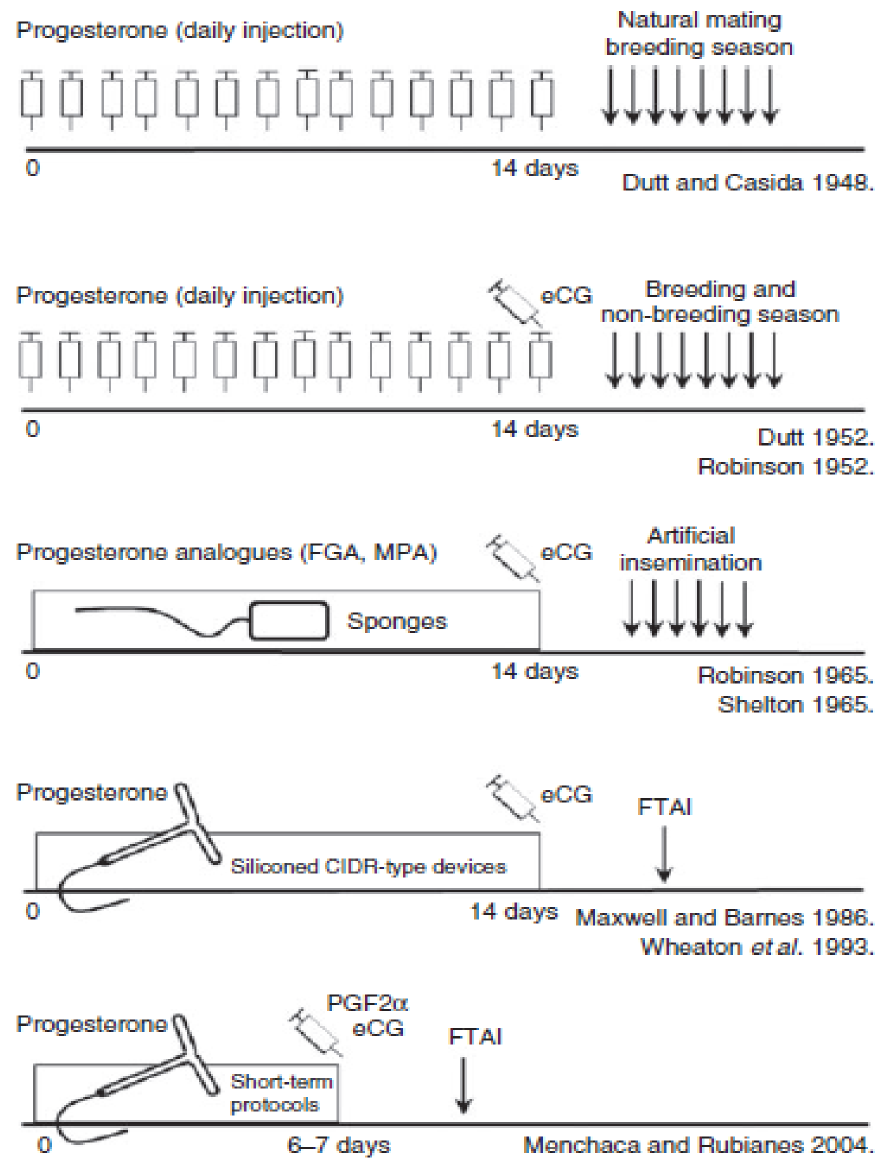
**Table 4.** Estrus response within 96 h and fertility in sheep synchronized with the use of daily feeding of an MGA supplement

| Daily dose, mg | Feeding duration, d | Associated treatment | Breed | Season | n | Estrus, % | Mating system | Fertility, % | Litter size | Reference |
|---|---|---|---|---|---|---|---|---|---|---|
| .25 | 14 | None | Mixed | Anestrus | 20 | 80.0 | Natural | 75.0$^{a}$ | 1.33 | Powell et al., 1996 |
| | | 5 mg Zeranol 30 h after end of feeding | | | 23 | 95.7 | | 43.5$^{b}$ | 1.10 | |
| .25 | 8 | None | Rambouillet | Anestrus | 20 | 90.0 | Natural | 65.0 | 1.46 | Powell et al., 1996 |
| | 11 | | | | 21 | 71.4 | | 61.9 | 1.39 | |
| | 14 | | | | 26 | 92.3 | | 57.7 | 1.27 | |
| .25 | 8 | None | Mixed | Anestrus | 51 | 21.6$^{a}$ | Natural | 47.1$^{a}$ | 1.58 | Powell et al., 1996 |
| | | .315 mg Zeranol 30 h after end of feeding | | | 48 | 33.3$^{a}$ | | 39.6$^{ab}$ | 1.63 | |
| | | 1.25 mg Zeranol 30 h after end of feeding | | | 48 | 70.8$^{b}$ | | 29.2$^{ab}$ | 1.29 | |
| | | 5 mg Zeranol 30 h after end of feeding | | | 50 | 94.0$^{c}$ | | 12.0$^{b}$ | 1.17 | |
| .3 | 10 | None | Mixed | Anestrus | 14 | 57.0 | Natural | 64.0 | 1.33 | Umberger et al., 1994 |
| | | 400 IU PMSG/200 IU hCG at end of feeding | | | 14 | 43.0 | | 50.0 | 1.40 | |
| .3 | 10 | None | Mixed | Anestrus | 27 | 13.0 | Natural | 26.0 | 1.65 | Jabbar et al., 1994 |
| | | 2.5 mg Zeranol at beginning of feeding | | | 28 | 20.0 | | 50.0 | 1.61 | |
| | | 400 IU PMSG/200 IU hCG at end of feeding | | | 30 | 14.0 | | 36.0 | 1.68 | |
| .25 | 10 | None | Mixed | Anestrus | 39 | 55.2 | Natural | 40.5 | 1.91 | Safranski et al., 1992 |
| | | 400 IU PMSG/200 IU hCG at end of feeding | | | 38 | 69.8 | | 41.2 | 1.89 | |
| .22 | 14 | None | Mixed | Breeding | 48 | 74.0 | AI fresh | 27.7$^{a}$ | 1.3 | Quispe et al., 1994 |
| | | | | | 44 | | AI frozen | 11.6$^{b}$ | 1.3 | |

$^{a,b,c}$Values with unlike superscripts within same column and reference differ ($P < .05$).

# Progestagens

Seventy years of progestagen treatments in the ewe. **Since the first report in 1948**, progesterone and its analogues have been used to control the ovine oestrous cycle. **In the 1950s, daily progesterone injection treatment was associated with equine chorionic gonadotrophin (eCG) administration at the end of the protocol**, which allowed the synchronisation of ovulation during the breeding and non-breeding season. **In the 1960s, the main progress was the development of intravaginal sponges impregnated with the novel progesterone analogues flugestone (FGA) and medroxyprogesterone (MPA) acetate**. **In the 1980s and 1990s, the evolution in controlled drug releasing systems** enabled the design of silicone CIDR-type devices. Finally, **in the 2000s the protocols for fixed-time artificial insemination (FTAI) were reduced to 6–7 days and nowadays they have been validated during the breeding and non-breeding season,** with cervical, transcervical and intrauterine insemination, using both fresh and frozen semen.



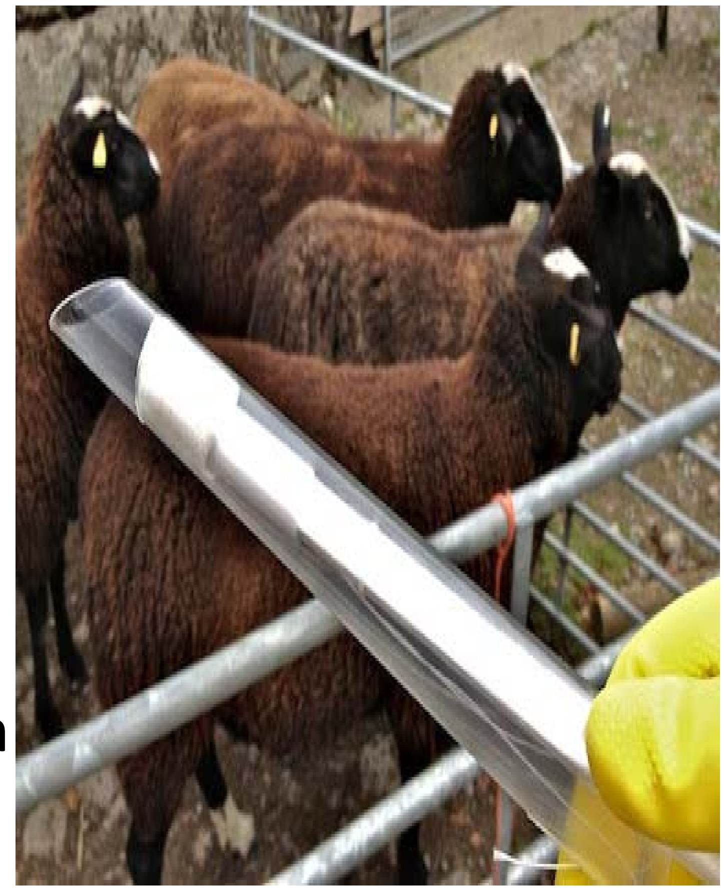
# Sponge

**Two types of sponges:**

- <u>Flurogestone Acetate (FGA),</u> marketed as Chronogest (Intervet, Angers, France)
- <u>Medroxyprogesterone Acetate (MAP),</u> marketed as Veramix (Pharmacia & Upjohn, Orangeville, Canada)

# Sponge Application

- Sponges are usually inserted over periods of **9 to 19 d in sheep and goat** and used in conjunction with PMSG, particularly for **out-of-season breeding**.
- PMSG injection at time of sponge removal or 48 h prior to sponge removal.
- Sponges have high retention rates (> 90%).
- Females usually exhibit estrus within 24 to 48 h after sponge removal.



# Efficacy of Intravaginal Sponges

- A comparison of intravaginal sponges containing 15, 30, 45, or **60** mg of MAP (**9 days duration+ Ram effect**) in seasonally **anovular** Corriedale ewes (n=278) showed no differences between doses in the percentage of **does** ovulating (96.8%) or in ovulation rate (1.25) (Iglesias et al., 1997).
- Lambing rate ranged 70-81% in different doses of MAP
- These findings suggest that MAP doses of 25% of the commercial formulation (60 mg) may still be sufficient to induce estrus in this breed.

**Table 1.** Estrus response within 96 h and fertility in does and ewes synchronized with FGA and MAP intravaginal sponges during anestrous and the breeding season not designed to achieve superovulation

| Type | Duration, d | Dose, mg | Associated treatment | Breed | n | Estrus, % | Mating system | Fertility, % | Litter size | Reference |
|---|---|---|---|---|---|---|---|---|---|---|
| Anovular does | | | | | | | | | | |
| FGA | 11 | 45 | 400 IU PMSG and 100 µg cloprostenol 48 h before sponge removal | Saanen | 169 | 80.7 | Hand-mating | 49.5 | — | Baril et al., 1992 |
| | | | | | | | AI | 62.8 | — | |
| FGA | 14 | 45 | FSH 12 mg, 8 injections at sponge removal | Dairy | 17 | 88 | — | — | — | Pendleton et al., 1992 |
| MAP | 14 | 60 | None | Boer | 15 | 53.5 | — | — | — | Greyling and Van Niekerk, 1991 |
| | 8 | | 62.5 µg cloprostenol at sponge removal | | 15 | 86.7 | — | — | — | |
| | 8 | | 500 IU PMSG and 62.5 µg clomprestenol at sponge removal | | 15 | 86.7 | — | — | — | |
| FGA | 16 | 40 | None | Nubian | 10 | 70.0 | Cervical AI | 40 | 1.5 | Ahmed et al., 1998 |
| | | | 300 IU PMSG at sponge removal | | 10 | 77.7 | | 33 | 1.6 | |
| FGA | 11 | 45 | 400 IU PMSG and 50 µg cloprostenol 48 h before sponge removal | Dairy | 640 | 98.1 | Timed AI | 65 | 1.9 | Baril et al., 1993 |
| FGA | 11 | 45 | 400 IU PMSG and 50 µg cloprostenol 48 h before sponge removal | Alpine | 15 | 93.8 | Cervical AI | 87.5 | 2.3 | Freitas et al., 1996b |
| | | | | Saanen | 17 | 100 | | 58.8 | 1.6 | |
| MAP | 17 | 60 | 400 IU PMSG 48 h before sponge removal | Dairy | 76 | | Natural | 53.9 | 2.3 | Robin et al., 1994 |
| FGA | | 45 | | | 78 | | | 43.6 | 2.2 | |
| Cyclic does | | | | | | | | | | |
| FGA | 18 | 45 | 200 IU at sponge removal | Cashmere | 198 | — | Cervical AI | 37.4 | 1.92 | Ritar et al., 1990 |
| | | | | | 279 | — | Laparo. AI | 62.7 | 1.73 | |
| MAP | 12 | 60 | None | Nubian | 10 | 100 | — | — | — | Romano, 1998b |
| FGA | | 30 | | | 14 | 100 | — | — | — | |
| MAP | 17 | 60 | 400 IU PMSG 48 h before sponge removal | Saanen | 6 | 100 | Cervical AI | 50 | — | Menegatos et al., 1995 |

| Type | Duration, d | Dose, mg | Associated treatment | Breed | n | Estrus, % | Mating system | Fertility, % | Litter size | Reference |
|---|---|---|---|---|---|---|---|---|---|---|
| Anovular ewes | | | | | | | | | | |
| MAP | 14 | 60 | 500 IU PMSG at sponge removal | Mixed | 167 | 94.1 | Natural | 65.0 | 1.67 | Tritschler et al., 1991 |
| FGA | 12 | 40 | 500 IU PMSG at sponge removal | Dorset | 12 | 77.0 | Natural | 53.0 | 1.01 | Rajamahendran et al., 1993 |
| FGA | 14 | 40 | None | Black Thibar | 40 | — | — | 57.5[a] | 1.30[a] | Zaiem et al., 1996 |
| | | | 300 IU PMSG at sponge removal | | 32 | — | — | 84.4[b] | 1.33[ab] | |
| | | | 450 IU PMSG at sponge removal | | 32 | — | — | 84.4[b] | 1.55[b] | |
| | | | 600 IU PMSG at sponge removal | | 32 | — | — | 81.2[b] | 1.77[b] | |
| MAP | 9 | 15 | Ram introduction | Corriedale | 58 | 90.7 | — | 81.8 | — | Iglesias et al., 1997 |
| | | 30 | | | 58 | 98.1 | — | 70.9 | — | |
| | | 45 | | | 58 | 94.1 | — | 76.0 | — | |
| | | 60 | | | 58 | 96.4 | — | 76.0 | — | |
| Cyclic ewes | | | | | | | | | | |
| MAP | 14 | 60 | None | Dwarf | 6 | 100 | — | — | — | Oyediji et al., 1990 |
| FGA | 12 | 40 | None | Menze | 12 | 83.3 | Natural | 75 | 1.11 | Mutiga and Mukasa-Mugerwa, 1992 |
| | | | 200 IU PMSG at sponge removal | | 12 | 100 | | 75 | 1.22 | |
| | | | 300 IU PMSG at sponge removal | | 12 | 75 | | 75 | 1.55 | |
| MAP | 14 | 60 | 200 IU PMSG at sponge removal | Merino | 1824 | 80.1 | Laparo. AI | 61 | — | Moses et al., 1997 |
| FGA | 14 | 30 | 400 IU PMSG at sponge removal | Merino | 116 | 96.7 | AI frozen | 39.3 | — | Tekin et al., 1992 |
| | | | | | | | AI fresh | 80.4 | — | |

[a,b]Values with unlike superscripts within same column and reference differ ($P < .05$).

# CIDR

- Silicone elastomers impregnated with progesterone
- CIDR-S and CIDR-G (InterAg, Hamilton, New Zealand); P4 content ranges from 9 to 12% (330 mg progesterone)
- Peak plasma P4 values of 2.1 ng/mL within 24 h and relatively stable levels between d 1 and 13 (1.9 ng/mL).

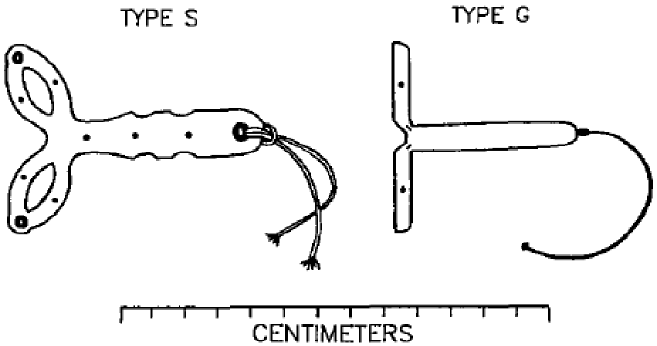



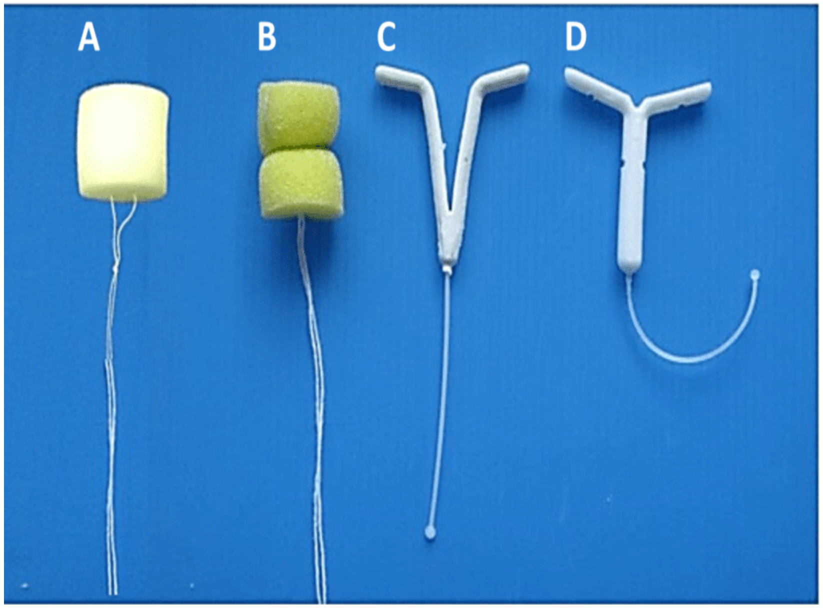

Fig. 1. Type S and G controlled internal drug release dispensers (CIDR).

# CIDR Application

- GOATS: Insert the device for **17–19 days**. For tighter synchrony and increased multiple births, eCG (PMSG) may be administered at the time of device removal.
- SHEEP: During the breeding season, insert the device for 12–14 days. Outside the breeding season, the device can be inserted for 7–12 days with eCG (PMSG) administered at the time of device removal.
- **Laparoscopic AI at 40–48 h after device removal in does** and **50–54 hours in ewes**. Cervical AI to detected oestrus. Buck/ram ration of at least 1:10 for natural mating.

# Efficacy of CIDR Devices

No differences between FGA sponges and CIDR devices (Ritar et al.,1990; n=1833 Cashmere Does)




Considerations:

- Price
- Retention Rate (97 vs 99%)
- Vaginitis
- Fertility?

**Table 2.** Estrus response within 96 h and fertility in goats and sheep synchronized with CIDR devices

| Type | Duration, d | Associated treatment | Breed | Season | n | Estrus, % | Ovulation rate | Mating system | Fertility, % | Litter size | Reference |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Sheep | | | | | | | | | | | |
| CIDR-S | 12 | None | Mixed | Breeding | 129 | 91 | — | Natural | 95.0 | — | Carlson et al., 1989 |
| CIDR-S | 14 | 750 IU PMSG at removal | Mixed | Anestrus | 165 | 92 | — | Natural | 64.0 | 1.00 | Hamra et al., 1989 |
| CIDR-G | 15–20 | 200 IU PMSG at removal | Mixed | Breeding | 204 | — | — | Cervical | 40.7 | 1.75 | Ritar et al., 1990 |
| | | | | | 290 | — | — | laparosc. | 64.5 | 1.84 | |
| | | | | | 479 | — | — | Laparosc. – 39 h | 51.6 | 1.27 | |
| | | | | | 383 | — | — | Laparosc. – 45 h | 52.7 | 1.20 | |
| CIDR-G | 12 | None | Mixed | Breeding | 29 | — | 1.40 | Natural | 72.0 | 1.20 | Godfrey et al., 1997 |
| | | | St. Croix | | 14 | — | — | Natural | 100 | 2.20 | |
| Goats | | | | | | | | | | | |
| CIDR-G | 16 | 250 IU PMSG 48 h before removal | Spanish | Breeding | 59 | — | — | Laparosc. | 64.5 | 1.70 | Waldron et al., 1999 |
| | | 250 IU PMSG + 5 mg PGF 48 h before removal | | | 59 | — | — | Laparosc. | 59.5 | 1.67 | |
| CIDR-G | 16–20 | 200 IU PMSG at removal | Cashmere | Breeding | 22 | 55 | 2.18 | — | — | — | Ritar et al., 1989 |
| | | 200 IU PMSG 48 h before removal | | | 22 | 95 | 2.68 | — | — | — | |
| CIDR-G | 16–18 | 200–400 IU PMSG at removal | Cashmere | Breeding | 14 | 92 | 2.15 | — | — | — | Ritar et al., 1994 |
| | | | Angora | | 6 | 50 | 1.33 | — | — | — | |

# Norgestomet Implants

**Table 3.** Estrus response within 96 h and fertility in goats and sheep synchronized in norgestomet implant-based systems not designed to achieve superovulation

| Dose, mg | Duration, d | Associated treatment | Breed | Season | n | Estrus, % | Mating system | Fertility, % | Litter size | Reference |
|---|---|---|---|---|---|---|---|---|---|---|
| Sheep | | | | | | | | | | |
| 2 | 14 | 500 IU PMSG at removal | Mixed | Anestrus | 128 | 96 | Natural | 59 | 1.44 | Tritschler et al., 1991 |
| 3 | 14 | 6 mg FSH-P, graded doses | Mixed | Anestrus | 25 | 48 | Natural | 40 | | Youngs, 1992 |
| 3 | 10 | None | Mixed | Anestrus | 14 | 93 | Natural | 50 | 1.83 | Umberger et al., 1994 |
| | | 400 IU PMSG/200 IU hCG at removal | | | 14 | 71 | | 50 | 1.90 | |
| 3 | 10 | None | Mixed | Anestrus | 29 | 72 | Natural | 45 | 1.71 | Jabbar et al., 1994 |
| | | 400 IU PMSG/200 IU hCG at removal | | | 29 | 90 | | 59 | 1.88 | |
| Goats | | | | | | | | | | |
| 3 | 11 | 500 IU PMSG and 50 µg cloprostenol 24 h before removal | Dairy | Anestrus | 62 | 97 | Natural | 60 | | Bretzlaff and Madrid, 1989 |
| | | | | | | | Cervical AI | 27 | | |
| 3 | 9 | None | Dairy | Breeding | 6 | 100 | Natural | 83 | | Bretzlaff et al., 1991 |
| 3 | 9 | 250 IU PMSG 48 h before removal | Dairy | Transition | 45 | 93 | Hand-mating | 64 | | East and Rowe, 1989 |
| 2 | 9 | 1.25 mg estradiol at implantation | Criollo | Breeding | 42 | 62 | | | | Mellado and Valdez, 1997 |
| 1.5 | | | | | 42 | 62 | | | | |
| 1.2 | | | | | 42 | 55 | | | | |
| 3 | 11 | 400 IU PMSG and 50 µg cloprostenol 48 h before removal | Dairy | Breeding | 43 | 97 | | | | Freitas et al., 1997b |
| 1.5 | | | | | 39 | 98 | | | | |
| 3 | | | | Anestrus | 56 | 98 | Cervical AI | 75[a] | 1.9 | |
| 1.5 | | | | | 55 | 98 | | 45[b] | 1.8 | |
| 3 | 9–13 | 300 IU PMSG 36 h before and 50 µg cloprostenol at removal | Dairy | Transition | 67 | 89 | Hand-mating | 70 | 2.1 | Rowe and East, 1996 |
| 3 | 11 | 400 IU PMSG and 50 µg cloprostenol 48 h before removal | Dairy | Breeding | 39 | 97 | | | | Freitas et al., 1996a |

**Table 1** Common and practical approaches for controlling estrus cycles and inducing ovulation in anovular or cycling goats[a]

| *Protocol*[b] | *Estrus response (%)* | *Onset of standing estrus (h)* | *Conception or kidding rate (%)* |
|---|---|---|---|
| 2 injections $PGF_{2\alpha}$ 10-14-d apart | 84–94 | 52–55 | 55–75 |
| FGA 16-d/eCG 200–250 IU | 95 | – | 58 |
| FGA 11-21-d/eCG 400 IU/$PGF_{2\alpha}$ | 96 | 33 | 32–67 |
| MAP 13-17-d/eCG 300–500 IU | 90–100 | 35 | 41–81 |
| MAP 9-19-d/eCG 200–500 IU/$PGF_{2\alpha}$ | 97 | 23–81 | 50–71 |
| CIDR 11-d/eCG 200–600 IU | 70 | 40–50 | 53–75 |
| GnRH d 0/PGF2α d 7/GnRH d 9/TAI | 96 | – | 58 |
| MAP 6-d/PGF2α and eCG at d 5 | 90–100 | 27–28 | 60–72 |
| Buck stimulus | 79–92 | 110–115 | 82–85 |
| Buck stimulus/norgestomet 9-d | 92 | 54 | 78 |
| Norgestomet 9-d/eCG 100 UI | 100 | – | 80 |
| Sterile copulation/FGA 12-d | 70 | 40–50 | 53–75 |
| ♂ effect/P at ♂ exposure/$PGF_{2\alpha}$ 9 d later/TAI | 88 | 37 | 66 |
| $PGF_{2\alpha}$ d-1 + MAP 5-d/250 IU eCG at d-5/TAI | 92 | 54 | 64 |

FGA — fluorogestone acetate; CIDR — controlled internal drug release device (releases progesterone); eCG — equine chorionic gonadotrophin; MAP — medroxy progesterone acetate; P — progesterone; GnRH — gonadotrophin releasing hormone; TAI — timed artificial insemination; d — day.

[a]From the literature.

[b]$PGF_{2\alpha}$ — prostaglandin $F_{2\alpha}$ analogs.

# PMSG

Pregnant Mare Serum Gonadotropin

- A gonadotropic hormone produced in the chorion of pregnant mares
- In equids PMSG has only LH like activity, but in other species it has activity like both FSH and LH.
- limitation of PMSG is its long-acting biological activity, which results in a large number of unovulated follicles when given at higher doses.
- Various studies have evaluated **different dose** levels of PMSG, the **timing of PMSG** treatment, and **alternative types of gonadotropins**.

# PMSG Dosage?

- Three doses of PMSG (300, 450, and 600 IU) were evaluated for use with **FGA (40 mg, 14 d)** sponges during the **anestrous season in ewes** (Zaiem et al., 1996).
- All three PMSG dose levels yielded similar fertility rates **(81.2 to 84.3%)** that were higher than those in FGA-treated control ewes receiving **no gonadotropin (57.5).**
- Prolificacy was increased over that of **controls (130.4%) at PMSG dose levels of 450 IU (155.5%) and 600 IU (176.9%),** but not at 300 IU (133.3), suggesting that 450 to 600 IU PMSG are **optimal levels** in this scenario.

Trop Anim Health Prod. 2011 Dec;43(8):1567-73. doi: 10.1007/s11250-011-9843-z.
Epub 2011 Apr 5.

# The effects of time and dose of pregnant mare serum gonadotropin (PMSG) on reproductive efficiency in hair sheep ewes

PMSG
Timing???

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PMID: 21465100 DOI: 10.1007/s11250-011-9843-z

## Abstract

The aim of this study was to evaluate the effects of dose and application time of pregnant mare serum gonadotropin (PMSG) on reproductive performance of hair sheep ewes synchronized with fluorogesterone acetate (FGA) under tropical conditions of Northeastern Mexico. Ninety-nine hair ewes (63 Blackbelly and 36 Pelibuey) were treated with intravaginal sponges during 10 days. After insertion of FGA sponges, ewes were divided into four groups, and PMSG was injected intramuscularly at doses of 100, 200, and 400 IU. Relative to FGA sponge removal, PMSG was administrated at -48 h, -24 h, and at sponge removal. PMSG was not administered to the control group. Control ewes had similar ($P > 0.05$) lambing rate, fertility, and fecundity than those treated with 100 IU of PMSG, but lower ($P < 0.05$) percentages to these variables than those treated with 200 and 400 IU of PMSG. Time to estrus decreased linearly, and ovulation rate increased quadratically as PMSG dose increased (0 to 400 IU). Administration of PMSG before sponge removal increased ($P < 0.01$) response to estrus and decreased ($P < 0.01$) interval to estrus compared with control. Ovulation rate, lambing rate, fertility, and fecundity were not affected ($P > 0.05$) by administration time of PMSG. Both dose and time of PMSG application did not affect ($P > 0.05$) pregnancy rate, percentage of single and multiple lambing, and prolificacy. In conclusion, results show that the dose of 400 IU of PMSG administered before sponge withdrawal in an estrus

Small Ruminant Research
Volume 56, Issues 1–3, January 2005, Pages 47-53


# Effect of progestagen and PMSG on oestrous synchronization and fertility in Dorper ewes during the transition period

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- Two types of intravaginal progestagen sponges, namely MAP (60 mg) (*n*=102) and FGA (40 mg) (*n*=100), three times of PMSG administration relative to sponge withdrawal (24 h before (*n*=59), at (*n*=56) or 24 h after (*n*=57)) and two routes of PMSG administration (intramuscular (*n*=87) or subcutaneous (*n*=85)) were compared regarding synchronization efficiency (oestrous response, time to onset of oestrus and duration of oestrus) and fertility (pregnancy, lambing, and fecundity rates) following AI with 0.1 ml fresh diluted semen.

- Within treatment, pregnancy, lambing, and fecundity rates were significantly higher in ewes administered 300 IU PMSG 24 h prior to (78.0, 115.3, and 147.8%, respectively) or at sponge withdrawal (75.0, 94.6, and 126.2%, respectively), compared to those administered 24 h after sponge withdrawal (70.2, 73.7, and 105.0%, respectively)

Table 1. Common and practical approaches for controlling estrus cycles and inducing ovulation in anovular or cycling goats. Data from the literature

| Protocol | Estrus response (%) | Onset of standing estrus (h) | Pregnancy or kidding rate (%) |
|---|---|---|---|
| 20 mg $P_4$ D0, 100 IU hCG D1 | 90–100 | 52–60 | 56–100 |
| 2 Injections $PGF_{2\alpha}$ 10–14-d apart | 84–94 | 52–55 | 55–75 |
| $PGF_{2\alpha}$ D0, GnRH d7, $PGF_{2\alpha}$ D14, GnRH d17 | 73 | | 68 |
| 4 µg GnRH d0, 3.75 mg $PGF_{2\alpha}$ D7, 4 µg GnRH D9 | 75–100 | 45–50 | 58 |
| CIDR 11-d/eCG 200–600 IU | 70 | 40–50 | 53–75 |
| FGA 16-d/eCG 200–250 IU | 95 | – | 58 |
| FGA 11–21-d/eCG 400 IU/$PGF_{2\alpha}$ | 96 | 33 | 32–67 |
| MAP 13–17-d/eCG 300–500 IU | 90–100 | 35 | 41–81 |
| MAP 9–19-d/eCG 200–500 IU/$PGF_{2\alpha}$ | 97 | 23–81 | 50–71 |
| CIDR 11-d/eCG 200–600 IU | 70 | 40–50 | 53–75 |
| MAP 6-d/PGF2α and eCG at d 5 | 90–100 | 27–28 | 60–72 |
| Buck stimulus | 79–100 | 110–115 | 82–85 |
| Buck stimulus/norgestomet 9-d | 92 | 54 | 78 |
| Norgestomet 9-d/eCG 100 UI | 100 | – | 80 |
| Sterile copulation/FGA 12-d | 70 | 40–50 | 53–75 |
| ♂ effect/P at ♂ exposure/$PGF_{2\alpha}$ 9 d later/TAI | 88 | 37 | 66 |

# GnRH (Gonadorelin)

Gonadotrophin Releasing Hormone;
- Gonadorelin Diacetate Tetrahydrate
- Gonadorelin Hydrochloride

**Commercial products**:

-Cystorelin (Gonadorelin Diacetate Tetrahydrate)

-Factrel (Gonadorelin Hydrochloride)

- Fertagyl (Gonadorelin Acetate)
- Ovacyst (Gonadorelin Diacetate Tetrahydrate)

*animals*

MDPI

*Article*

# Efficiency of CIDR-Based Protocols Including GnRH Instead of eCG for Estrus Synchronization in Sheep

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Received: 7 March 2019; Accepted: 1 April 2019; Published: 3 April 2019

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**Simple Summary:** This study examines the preovulatory and ovulatory events (in terms of the timing of onset of estrus behavior, preovulatory LH surge, and ovulation) and the yields obtained (in terms of ovulation rate, progesterone secretion, and fertility) after insertion of controlled internal drug release (CIDR) devices for 5 days and treatment with equine chorionic gonadotrophin (eCG) or gonadotrophin-releasing hormone (GnRH).

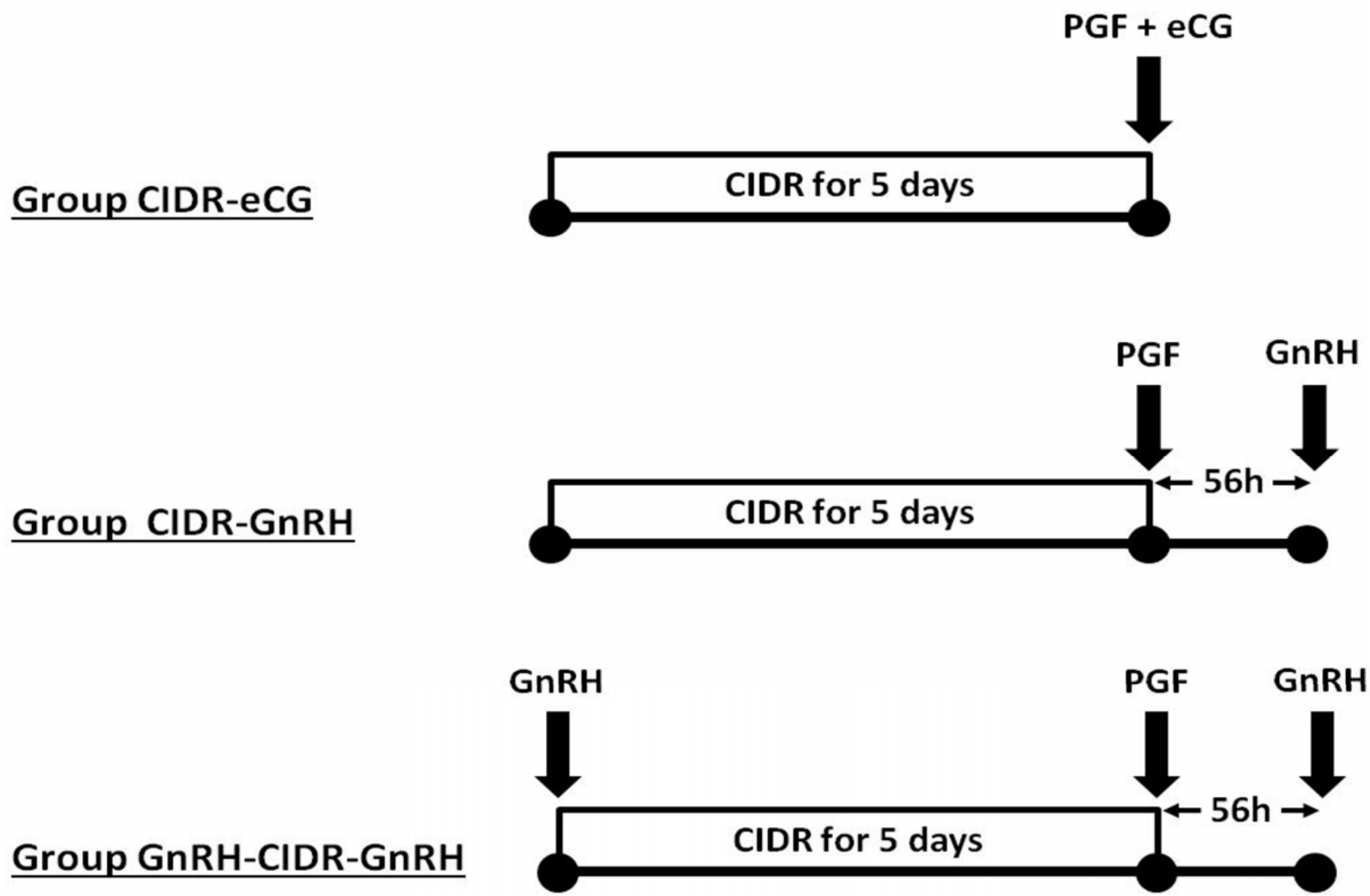

PGF + eCG
Group CIDR-eCG
CIDR for 5 days
PGF
GnRH
56h
Group CIDR-GnRH
CIDR for 5 days
GnRH
PGF
GnRH
56h
Group GnRH-CIDR-GnRH
CIDR for 5 days

**Table 1.** Percentage and timing of occurrence (hours ± SEM) of estrus behavior, preovulatory luteinizing hormone (LH) surge, and ovulation in ewes treated with a single i.m. dose of 400 IU of eCG at CIDR removal (group CIDR-eCG), with a single dose of GnRH at 56 h after CIDR removal (group CIDR-GnRH), and with two GnRH doses—one at CIDR insertion and one 56 h after CIDR removal (group GnRH-CIDR-GnRH).

| Event | CIDR-eCG (n = 19) | CIDR-GnRH (n = 19) | GnRH-CIDR-GnRH (n = 19) |
|---|---|---|---|
| Occurrence of estrus behavior (%) | 17/19 (89.5) | 17/19 (89.5) | 16/19 (84.2) |
| Timing of estrus behavior after CIDR removal (range) | 34.1 ± 2.0 [a] (24–44) | 39.3 ± 2.0 [b] (28–52) | 39.8 ± 2.2 [b] (24–52) |
| Occurrence of preovulatory LH surge (%) | 17/17 (100) | 17/17 (100) | 16/16 (100) |
| Timing of preovulatory LH surge after CIDR removal (range) | 42.2 ± 3.0 [a] (28–56) | 44.4 ± 2.3 [a,b] (32–52) | 50.7 ± 1.9 [b] (44–56) |
| Timing of preovulatory LH surge after onset of estrus behavior (range) | 8.0 ± 1.0 (4–12) | 6.7 ± 1.6 (4–16) | 7.5 ± 1.6 (4–16) |
| Occurrence of ovulation (%) | 17/17 (100) | 17/17 (100) | 16/16 (100) |
| Timing of ovulation after CIDR removal (range) | 65.8 ± 2.3 [a] (52–76) | 68.4 ± 2.5 [a,b] (60–80) | 73.8 ± 2.1 [b] (68–84) |
| Timing of ovulation after onset of estrus behavior (range) | 31.6 ± 0.8 (28–36) | 30.7 ± 0.9 (28–36) | 30.2 ± 1.0 (28–36) |
| Timing of ovulation after onset of preovulatory LH surge (range) | 24.0 ± 1.1 (16–28) | 24.0 ± 1.4 (16–28) | 22.5 ± 1.3 (16–28) |

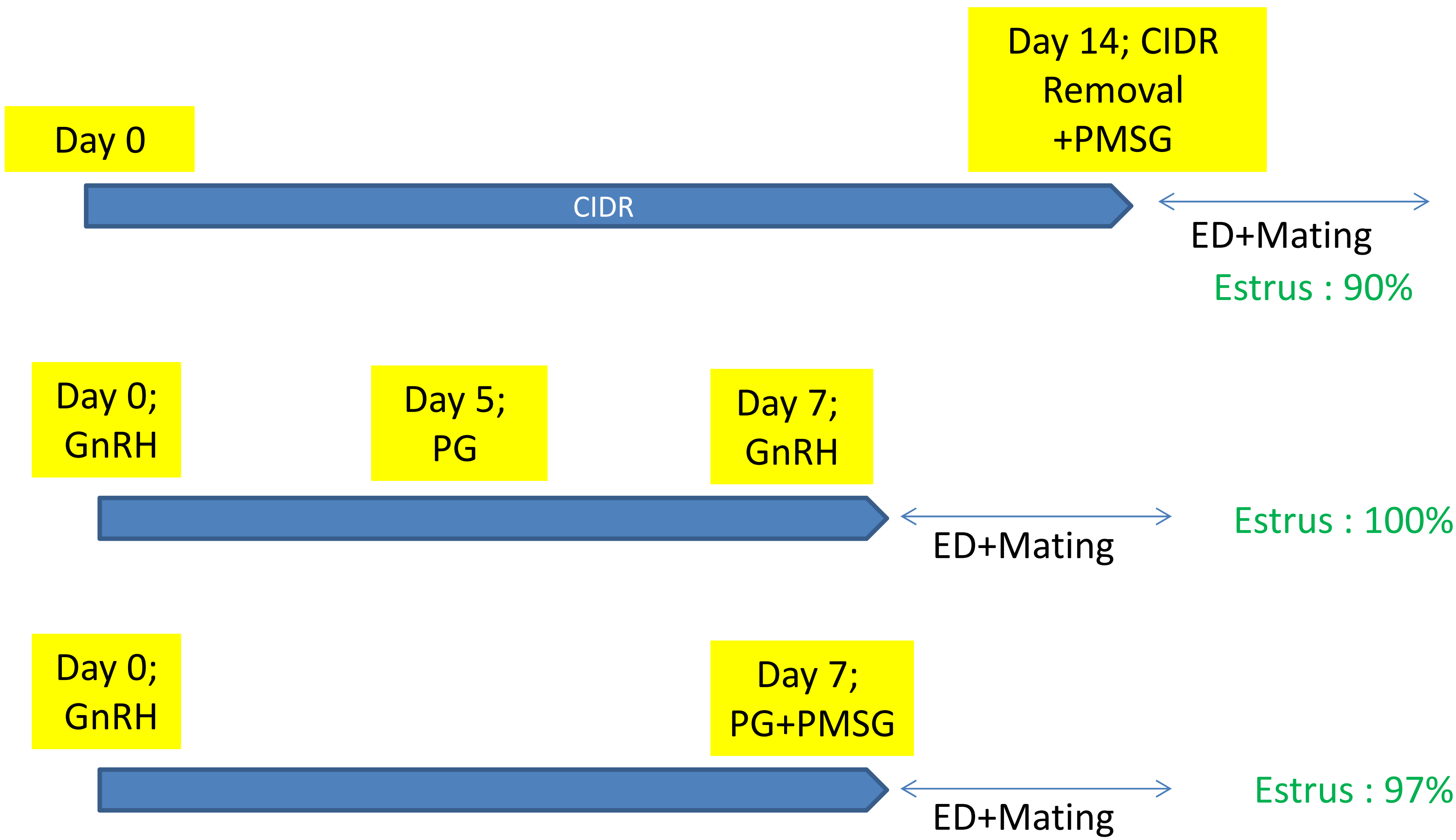
Different superscripts indicate significant differences among treatments (a ≠ b: $p < 0.05$).

**Table 2.** Mean (± SEM) number of corpora lutea and plasma progesterone concentrations (ng/mL) and fertility rate in ewes treated with a single i.m. dose of 400 IU of eCG at CIDR removal (group CIDR-eCG), with a single dose of GnRH at 56 h after CIDR removal (group CIDR-GnRH), and with two GnRH doses—one at CIDR insertion and one 56 h after CIDR removal (group GnRH-CIDR-GnRH).

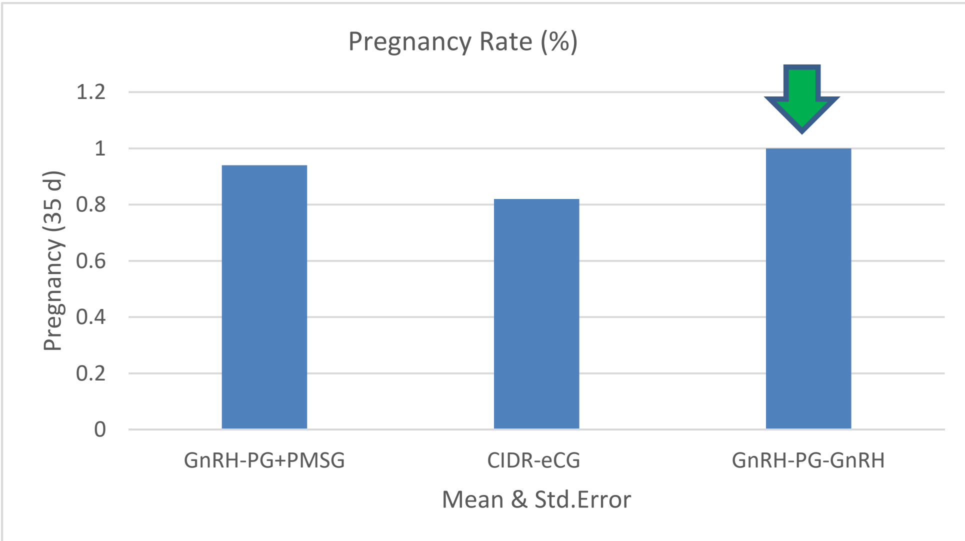
| Parameter | CIDR-eCG | CIDR-GnRH | GnRH-CIDR-GnRH |
|---|---|---|---|
| Number of corpora lutea (range) | $2.1 \pm 0.2^{a}$ (1–4) | $1.3 \pm 0.2^{b}$ (1–2) | $1.6 \pm 0.2^{a}$ (1–2) |
| Plasma progesterone concentrations (range) | 5.9 ± 1.0 (2.3–7.8) | 5.1 ± 0.6 (2.9–7.1) | 4.9 ± 0.7 (1.5–7.0) |
| Fertility rate with regards to ewes ovulating (%) | 13/17 (76.5) | 11/17 (64.7) | 13/16 (81.3) |
| Fertility rate with regards to treated ewes (%) | 13/19 (68.4) | 11/19 (57.9) | 13/19 (68.4) |

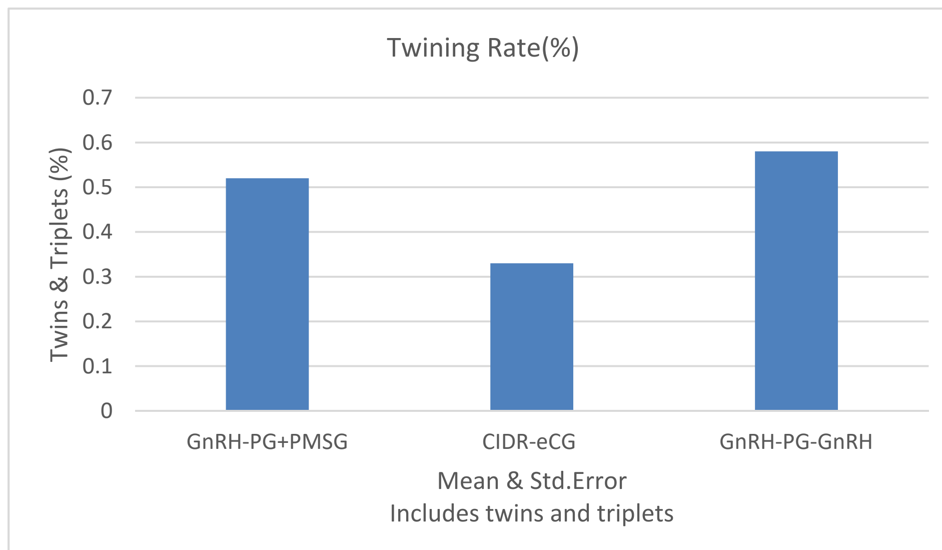
Different superscripts indicate significant differences among treatments (a ≠ b: $p < 0.05$).

In fact, the range of ovulations was narrower in the GnRH-CIDR-GnRH group, which suggests better synchronization of follicular growth ($p < 0.05$). In conclusion, protocols with two doses of GnRH offer similar yields to eCG protocols in breeding season (December).


Day 0
Day 14; CIDR Removal +PMSG
CIDR
ED+Mating
Estrus : 90%
Day 0; GnRH
Day 5; PG
Day 7; GnRH
ED+Mating
Estrus : 100%
Day 0; GnRH
Day 7; PG+PMSG
ED+Mating
Estrus : 97%

NO CIDR
NO PMSG



# $PGF_{2\alpha}$

- Prostaglandin-based ES systems control the estrous cycle by terminating the luteal phase through regression of the CL.
- The two commonly used products are **PGF2α** (**Lutalyse**; Pharmacia & Upjohn) and the prostaglandin analogue **cloprostenol** (**Estrumate**; Bayer, Shawnee Mission, KS).

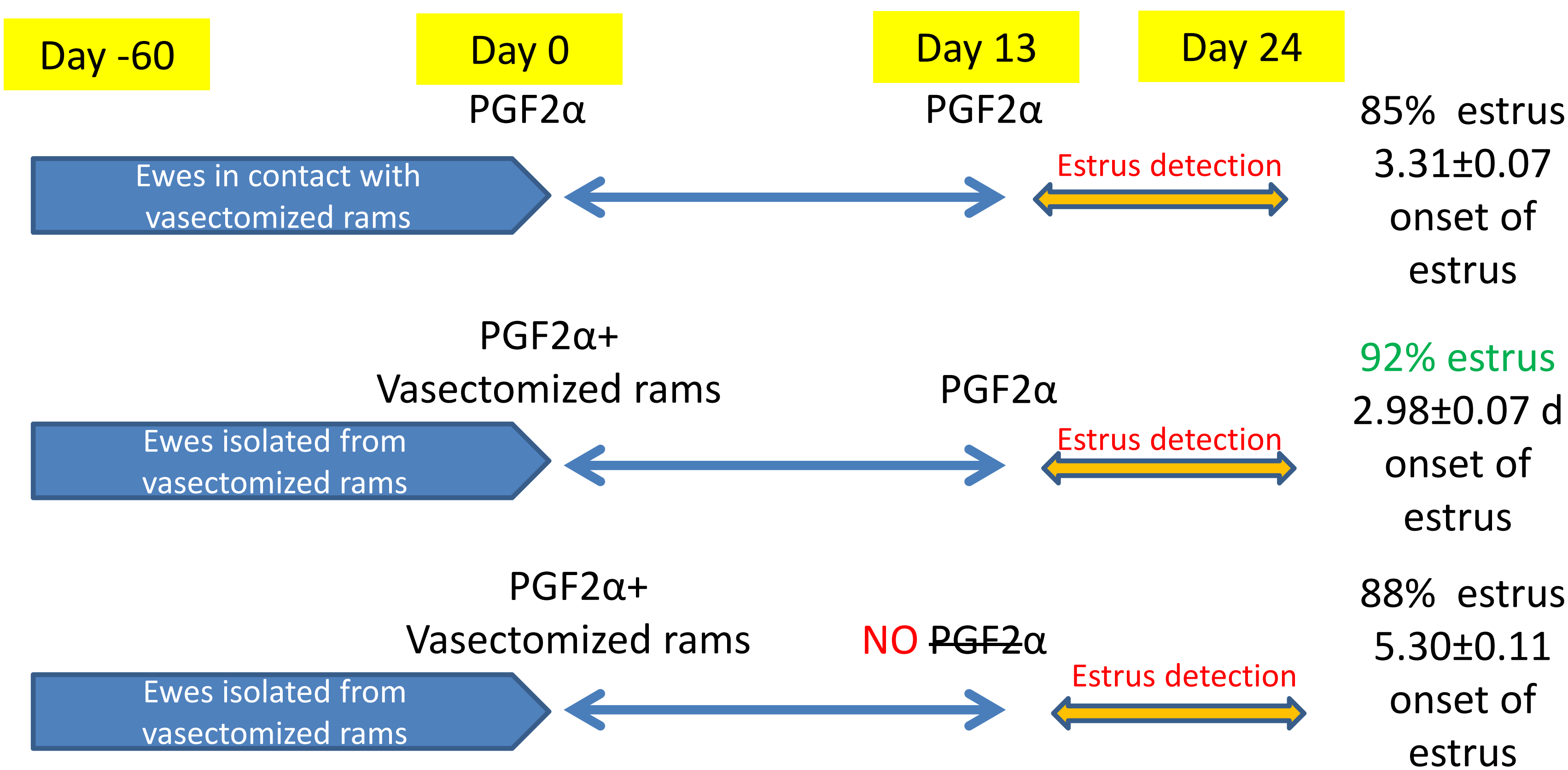

- In **cycling goats and ewes** estrus may be synchronized by two doses of $PGF_{2\alpha}$:
  - 11–13 days apart in DOE ($PGF_{2\alpha}$ 2.5–5 mg, IM) or cloprostenol (62.5–125 mcg, IM) as early as day 3
  - 7–9 days apart in EWE ($PGF_{2\alpha}$ ≥15 mg) or cloprostenol 125 mcg after day 5 of the cycle.

# 2× PGF2α + TAI

- A new protocol (Synchrovine) was proposed that would synchronise ovulation of the first follicular wave, **with two doses of PGF2a given 7 days apart followed by FTAI 42–48 h later** (Menchaca *et al. 2004).* Synchronised ovulation was greater than 90% but fertility was extremely low (e.g. less than 40%).
- A total of 436 nulliparous and multiparous ewes
- A single **cervical TAI with fresh undiluted semen** was performed either at 42h (n=152), 48h (n=120), or 54h (n=164), after the second PGF2$\alpha$ without taking into account the oestrous response.

# Ram effect + PGF2α

- Effective in cyclic Ewes and Does
- A total of 1264 Corriedale × Merino ewes in the breeding season (Ungerfeld , 2011)



# Ram effect + PGF2α

Cadena-Villegas et al., 2018.

Estrus synchronization in ewes with PGF2α and bio stimulated with “male effect”

- The sheep were randomly assigned to one of two treatments of the estrus synchronization protocol: T1, n = 25: synchronized sheep with **two doses of 250 µg of Cloprostenol via IM with interval of seven days** (PG, Control); and T2, n=28: similar to **T1, but with the "male effect" from fourth day to seventh day of the application of Cloprostenol.**

**Table 1. Estrus response in sheep synchronized with two doses of prostaglandins (PGF2α) and male effect (ME)**

| Variables | T1: PG | T2: PG+ME |
|---|---|---|
| n | 25 | 28 |
| Sheep in estrus (%) | 13 (52.0)a | 17 (60.7)a |
| Start of estrus (h) | 72.53 ± 6.05a | 45.13 ± 6.13b |
| Pregnant sheep | 12/25 (48.0)a | 15/28 (53.6)a |
| Lambed sheeps | 12/12 (100.0)a | 15/15 (100.0)a |
| Lambs born | 26 | 39 |
| Fertility | 12/25 (48.0)a | 15/28 (53.6)a |
| Prolificicacy | 26/12 (2.16)b | 39/15 (2.6)a |
| Fertility | 26/25 (1.04)b | 39/28 (1.40)a |

To assist in initiating hormonal events necessary to synchronize estrous cycles, such as estrus and ovulation, GnRH may also be incorporated, especially in anestrous ewes.

# Ram effect

- The "ram effect" is when **non-cycling ewes are stimulated to ovulate by the sudden introduction of a novel ram** or androgen treated castrates.
- For the ram effect to work, ewes should be isolated from rams for **at least 6 weeks**. Ewes must have no contact with rams by either sight, sound, or smell.
- This response is dependent on the depth of seasonal anestrus and associated with a **first ovulation in 2 to 3 d**.
- The **first ovulation is usually silent and of low fertility**, with a premature regression of the first CL. **The second ovulation 5 d later** is accompanied by a fertile estrus with a luteal phase of normal length.
- The primary limitation to the use of the male effect for ES is the **reduced fertility of the first cycle and the loss of synchrony in subsequent cycles.**

- **Exogenous progesterone (20 mg) at the time of male introduction significantly reduced the number of short estrus cycles** and extended the period from male induction to ovulation from 20. 5 to 58.8 h in sheep and increased ovulation rate in goats.
- Male effect for ES is most effective in anovular ewes.

# FSH

Exp 1. Chios at the **beginning of Breeding Season**

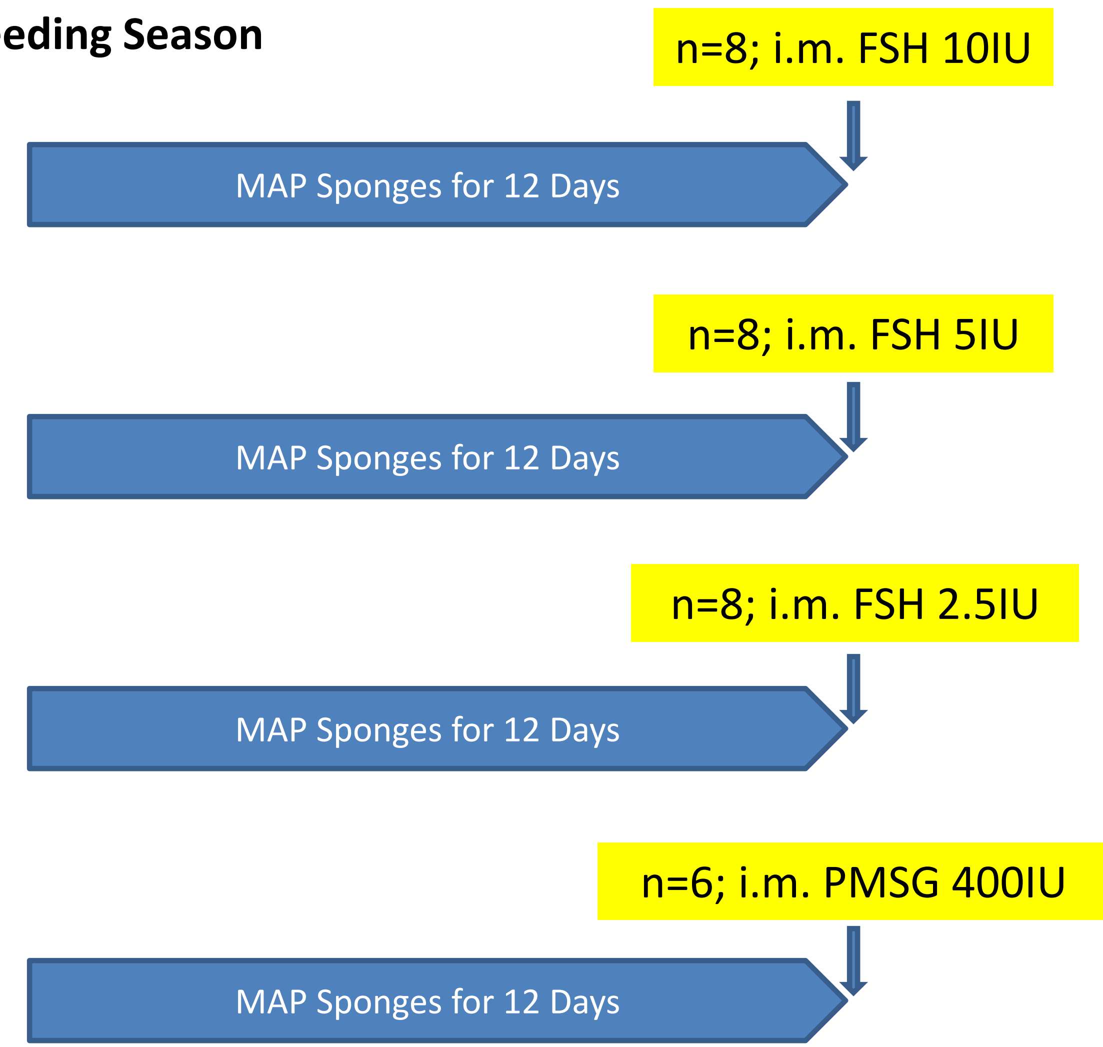


Table 1
Proportion of ewes in estrus and mean number of CL per ewe treated and per ewe ovulating, in the four treatment groups of Experiment I

| Treatment | Before treatment | After sponge withdrawal (Day 0) | | | | | |
|---|---|---|---|---|---|---|---|
| | Ewes with ovarian activity[1] | Days 2–4 | Day 2 | Day 10 | | | |
| | | Ewes in clinical oestrus | Ewes with $P_4 < 1.0$ ng/ml[2] | Ewes with $P_4 \geq 1.0$ ng/ml | Ewes with $\geq 1$ CL | CL per ewe treated | CL per ewe ovulating |
| Group 1 (10 IU FSH) | 37.5% (3/8) | 87.5% (7/8) | 100.0% (8/8) | 87.5% (7/8) | 87.5% (7/8) | $1.9 \pm 0.4$ | $2.1 \pm 0.3$ |
| Group 2 (5 IU FSH) | 37.5% (3/8) | 62.5% (5/8) | 100.0% (8/8) | 75.0% (6/8) | 75.0% (6/8) | $1.4 \pm 0.4$ | $1.8 \pm 0.4$ |
| Group 3 (2.5 IU FSH) | 37.5% (3/8) | 37.5% (3/8) | 75.0% (6/8) | 75.0% (6/8) | 75.0% (6/8) | $1.3 \pm 0.4$ | $1.7 \pm 0.4$ a |
| Group 4 (400 IU eCG) | 33.3% (2/6) | 33.3% (2/6) | 66.7% (4/6) | 100.0% (6/6) | 83.3% (5/6) | $2.3 \pm 0.5$ | $2.8 \pm 0.2$ b |
| TOTAL | 36.7% (11/30) | 56.7% (17/30) | 86.7% (26/30) | 83.3% (25/30) | 80.0% (24/30) | $1.7 \pm 0.2$ | $2.1 \pm 0.2$ |

Means in the same column with different letters (a, b) differ significantly ($P < 0.05$).

[1] Progesterone concentration $\geq 1.0$ ng/ml, in at least one of the three consecutive blood samplings before the beginning of Experiment I, was considered indicative of functional corpus luteum.

[2] $P_4$, serum progesterone concentration.

Exp 2. Chios & Berrichon ewes during mid breeding season

n=27 Chios & n=16 Berrichon; i.m. FSH 10IU

MAP Sponges for 12 Days

n=27 Chios & n=14 Berrichon; i.m. PMSG 400IU

MAP Sponges for 12 Days

Ewes in estrus were mated 2-4 and 19-23 days after sponge removal

Response of Chios and Berrichon ewes to estrus synchronization treatment with MAP intravaginal sponges plus 10 IU FSH or 400 IU eCG (Experiment II)

| Treatment | Ewes in clinical estrus on Days 2–4 after sponge removal | | | Ewes with $P_4 < 1.0$ ng/ml on Day 2 after sponge removal[1] | | |
|---|---|---|---|---|---|---|
| | Chios | Berrichon | Total | Chios | Berrichon | Total |
| Group 1 (10 IU FSH) | 88.9% (24/27) | 93.8% (15/16) | 90.7% (39/43) | 92.6% (25/27) | 100.0% (16/16) | 95.3% (41/43) |
| Group 4 (400 IU eCG) | 96.2% (25/26) | 85.7% (12/14) | 92.5% (37/40) | 96.2% (25/26) | 100.0% (14/14) | 97.5% (39/40) |
| Total | 92.5% (49/53) | 90.0% (27/30) | 91.6% (76/83) | 94.3% (50/53) | 100.0% (30/30) | 96.4% (80/83) |

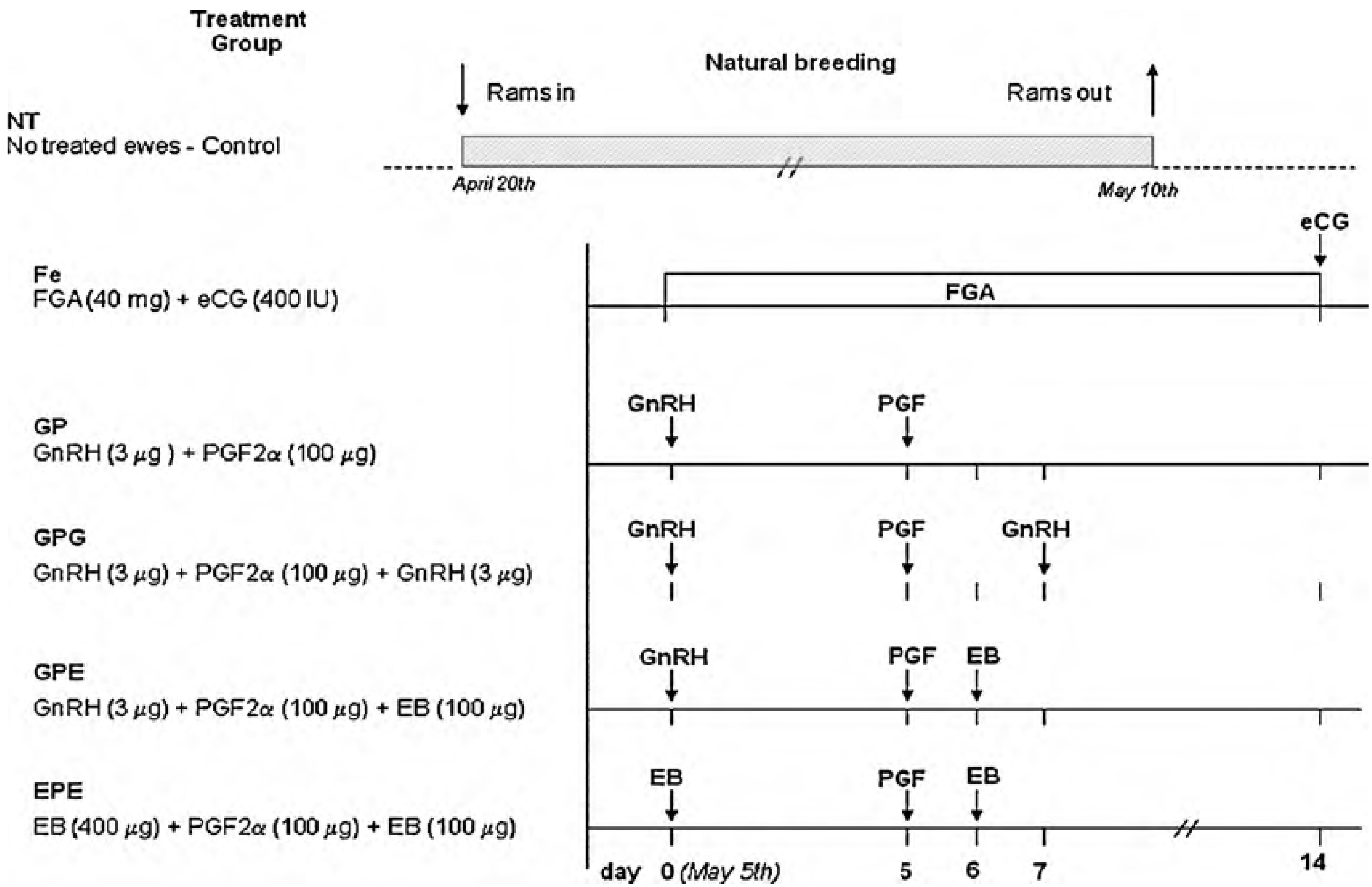
[1] $P_4$, serum progesterone concentration.

Overall (synchronization cycle and next cycle) lambing rate in Chios and Berrichon ewes after estrus synchronization with MAP intravaginal sponges plus 10 IU FSH or 400 IU eCG (Experiment II)

| Treatment | Chios | Berrichon | Total |
|---|---|---|---|
| Group 1 (10 IU FSH) | 63.0% (17/27) a | 93.8% (15/16) b, c | 74.4% (32/43) |
| Group 4 (400 IU eCG) | 80.8% (21/26) | 57.1% (8/14) d | 72.5% (29/40) |
| Total | 71.7% (38/53) | 76.7% (23/30) | 73.5% (61/83) |

Means in the same row with different letters (a, b) differ significantly ($P < 0.05$).
Means in the same column with different letters (c, d) differ significantly ($P < 0.05$).

# Short Term (5-7 days) GnRH, PG and Estradiol Benzoate Treatments in non-Breeding Season



**Fe**
FGA (40 mg) + eCG (400 IU)

**GP**
GnRH (3 µg ) + PGF2α (100 µg)

**GPG**
GnRH (3 µg) + PGF2α (100 µg) + GnRH (3 µ

**GPE**
GnRH (3 µg) + PGF2α (100 µg) + EB (100 µg

**EPE**
EB (400 µg) + PGF2α (100 µg) + EB (100 µg)

Effect of synchronization treatments on the oestrous response in ewes.

| Treatment group | Ewes in oestrus (%) | Occurrence of oestrus: hours after treatment ($x \pm SD$) |
|---|---|---|
| Fe | $93.3^{Aa}$ | $33.1^{A} \pm 4.28^{Ee}$ |
| GP | $46.7^{Db}$ | $41.1^{Bca} \pm 8.55^{fg}$ |
| GPG | $33.3^{B}$ | $59.2^{Bb} \pm 18.42^{Fh}$ |
| GPE | $62.5^{d}$ | $62.4^{Bd} \pm 12.39^{f}$ |
| EPE | $100^{Cc}$ | $49.1^{Bc} \pm 11.25^{f}$ |

Different superscripts in column differ significantly: A, B; B, C; C, D; E, F: $P < 0.01$; a, b; b, c; c, d; e, f; g, h: $P < 0.05$.

Fertility rates at induced oestrus for ewes treated with synchronization protocols and at the subsequent natural synchronized oestrus.

| Fertility[a] of NT group (control) (%) | Treatment group | Fertility at induced oestrus | | Prolificacy at induced oestrus[d] (%) | Fertility at natural oestrus following synchronized oestrus[e] (%) |
|---|---|---|---|---|---|
| | | Treated ewes[b] (%) | Ewes in oestrus[c] (%) | | |
| 36.7 | Fe | $60.0^{A}$ | $64.3^{Aa}$ | 155.5 | 50.0 |
| | GP | $33.3^{a}$ | $71.4^{a}$ | 140.0 | 50.0 |
| | GPG | $26.7^{a}$ | $80.0^{a}$ | 175.0 | 72.7 |
| | GPE | $12.5^{Bb}$ | $20.0^{Bb}$ | 100.0 | 64.3 |
| | EPE | – | – | – | 64.3 |

Different superscripts in column differ significantly, A, B: $P < 0.01$; a, b: $P < 0.05$.

[a] Number of ewes lambing/number of no treated ewes.
[b] Number of ewes lambing/number of ewes treated.
[c] Number of ewes lambing/number of ewes in oestrus and hand mated.
[d] Number of lambs born/number of ewes lambing.
[e] Number of ewes lambing at natural estrus following estrus synchronized/number of ewes treated not lambed at synchronized estrus.

**In the GPG group the fertility and prolificacy rates recorded were higher (80% and 175%), than in any of the other treatment groups.**

# Flushing

- Increasing the plane of nutrition for ewes 2 to 3 weeks prior to breeding and 3 weeks into the breeding season.
- Flushing works best on thin ewes (BCS < 2.0). Ewes that are already in good body condition (BCS > 3) usually do not respond well to flushing
- Supplementing Merino ewes with lupin grain (32% protein) starting d **8 of a 14-d FGA (40 mg) treatment** period resulted in a **64% increase *in ovulation rate*** *over* that in un-supplemented ewes (Pearse et al., 1994).
- It is more beneficial to flush **early or late in the breeding season**, when ovulation rates are naturally lower, compared to the middle of the breeding season.
- One pound of corn (90% TDN, 10% protein) can provide this extra energy (0.9 pound TDN) and protein (0.1 pound CP).

# Short ES protocols (5,6,7 day)

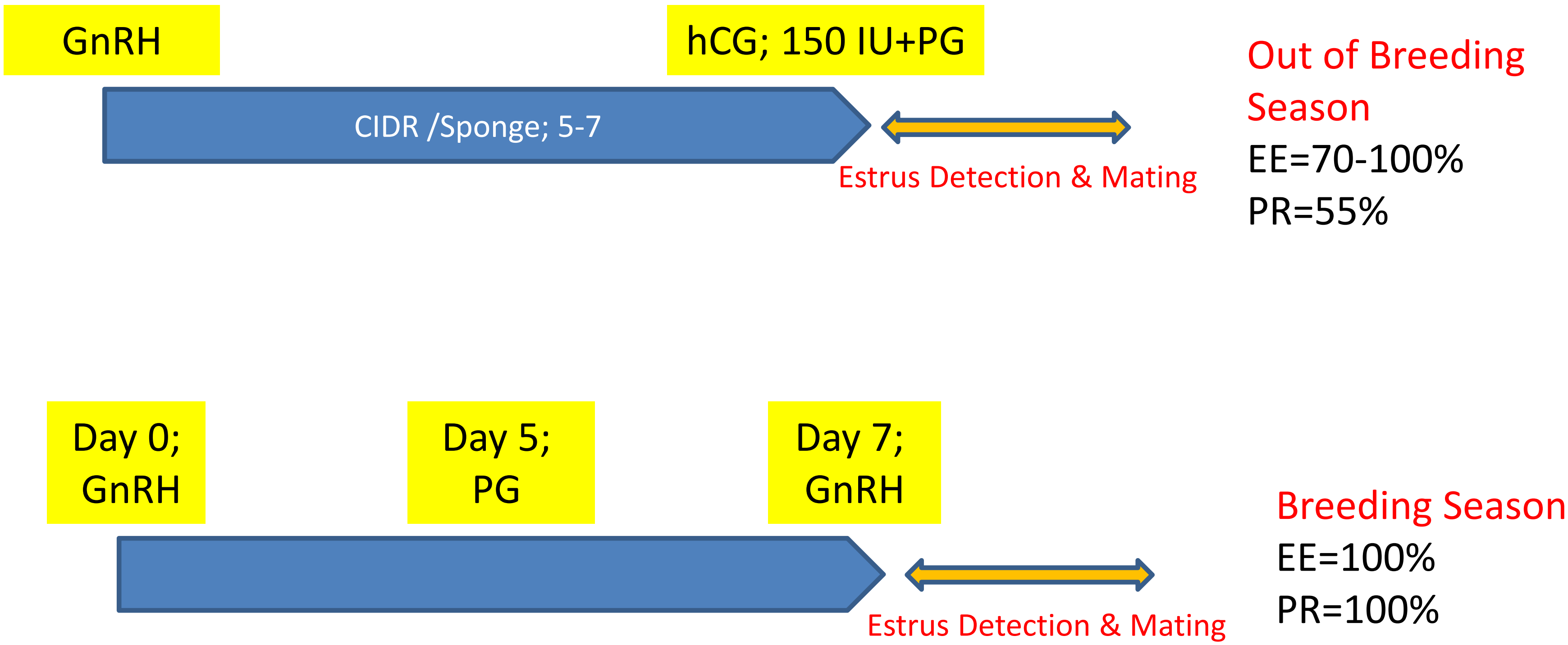
- Better control of follicular response and ovulation
- Acceptable fertility rates (no lower than conventional progesterone treatments)
- Shorter period for implementation of large scale FTAI programs
- Reutilization of intravaginal devices (CIDR)
- Less purulent or haemorrhagic fetid vaginal discharges at sponge removal (about 10% in short-term protocols and about 85% in long-term protocols)

# Moment of Ovulation and FTAI in Short Term ES Protocols

- The moment of ovulation after the Short-term protocol (i.e. CIDR by 5-7 days plus PGF and 250-300 IU eCG at device removal) occurs ~ 60 h from intravaginal device removal in sheep and goats.
- In 6 day protocol, intrauterine FTAI with frozen-thawed semen should be performed~52-56 h after CIDR removal and in Cervical FTAI with fresh semen ~46-50 h after CIDR removal.
- With re-used CIDR (2 to 3 times by 6 days) no differences were found between FTAI performed from 46 to 56 h with no interaction with the insemination by cervical or intrauterine route.

# Reuse of Intravaginal Devices

- Use of CIDR-G® and DICO® two or three times in a series of experiments conducted in sheep (Vilariño et al., 2010; 2013; dos Santos Neto et al., 2015).
- The proportion of sheep showing estrus and ovulation seems not to be affected by the devices used one, two or three times.
- However, pregnancy rate fell substantially with three times used devices in comparison with new ones, and was intermediate with second use devices.
- Similar results have been obtained in goats after exposure to progesterone intravaginal devices with this short treatment (Vilariño et al., 2011; Souza et al., 2011).
- In both species the insertion of new devices induce follicular turnover in all females, while with reused devices the treatment failed to induce a new follicular wave in about 20% of the females in which ovulation occurred from an older large follicle (Vilariño et al., 2011; 2013).
- With the short treatment of 6 days, even though pregnancy rate may be slightly reduced with reused devices, the decision to reuse the intravaginal devices require a case by case deep cost-benefit analysis.


GnRH
hCG; 150 IU+PG
CIDR /Sponge; 5-7
Estrus Detection & Mating
Out of Breeding Season
EE=70-100%
PR=55%
Day 0; GnRH
Day 5; PG
Day 7; GnRH
Estrus Detection & Mating
Breeding Season
EE=100%
PR=100%

# Considerations

- Body Condition Score (BCS)
- Seasonal breeding patterns
- Physiological status (Brood ewe or ewe-lamb, lactating or dry)
- Hormonal treatments (source and purity, dosage, duration, timing, route of administration, etc)
- Rations (protein, carbohydrate and fat requirements)
- Ram/Buck fertility
- Trace element and vitamin deficiency (copper, cobalt, selenium, manganese, iodine, zinc, iron , A, D, E)

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# Measures of Reproduction sheep

- estrus rate (ewes estrus/ewes mated × 100), lambing rate (ewes lambed/ewes mated × 100), infertility rate (infertile ewes/ewes exposed × 100), fecundity (lambs born/ewes mated), litter size (lambs born/number of lambing ewes), single lambing (single-born lambs/lambs born × 100), twin lambing (twins born/lambs born × 100), and survival rate (weaning lambs/lambs born × 100)