Journal club

Estrus synchronization in sheep

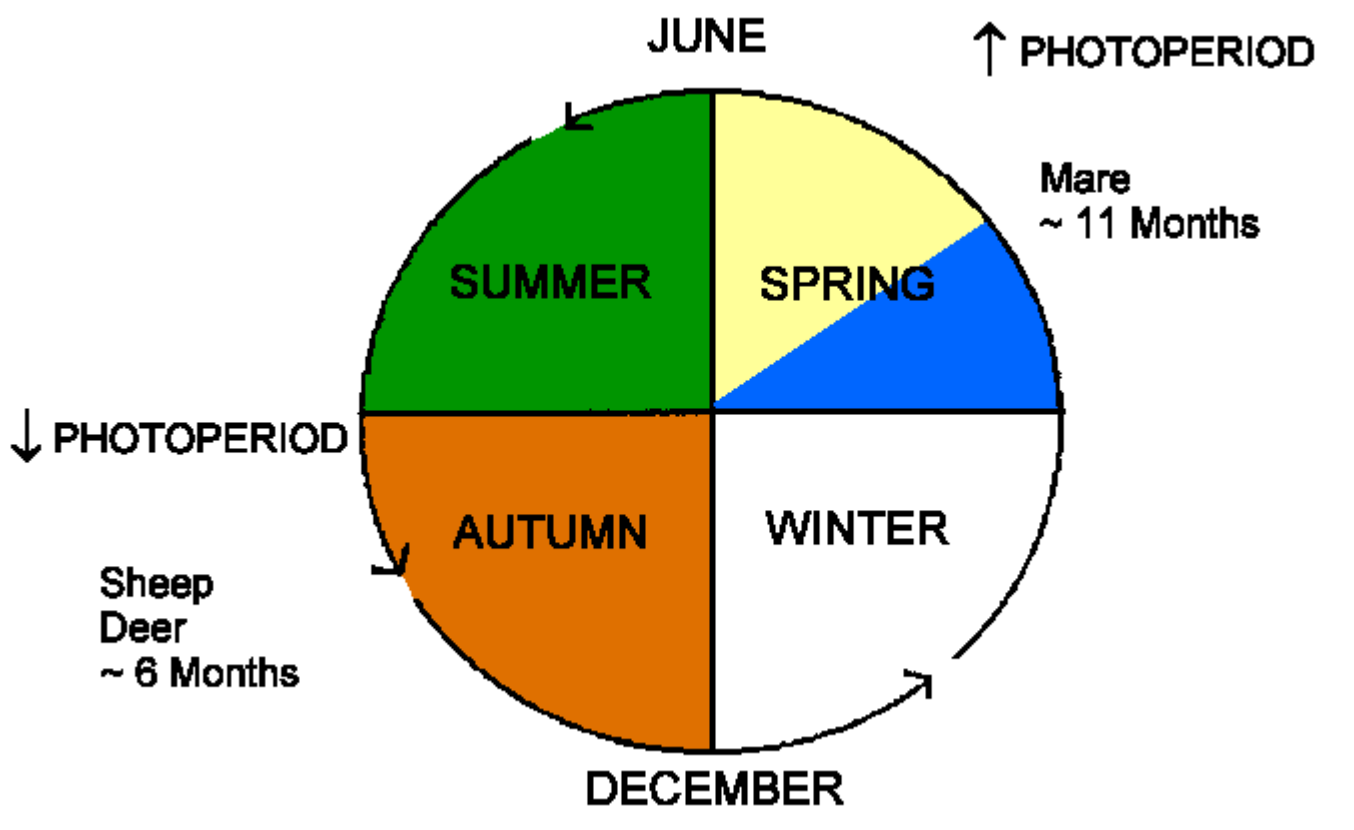
Chaiwat

Ewes reproductive

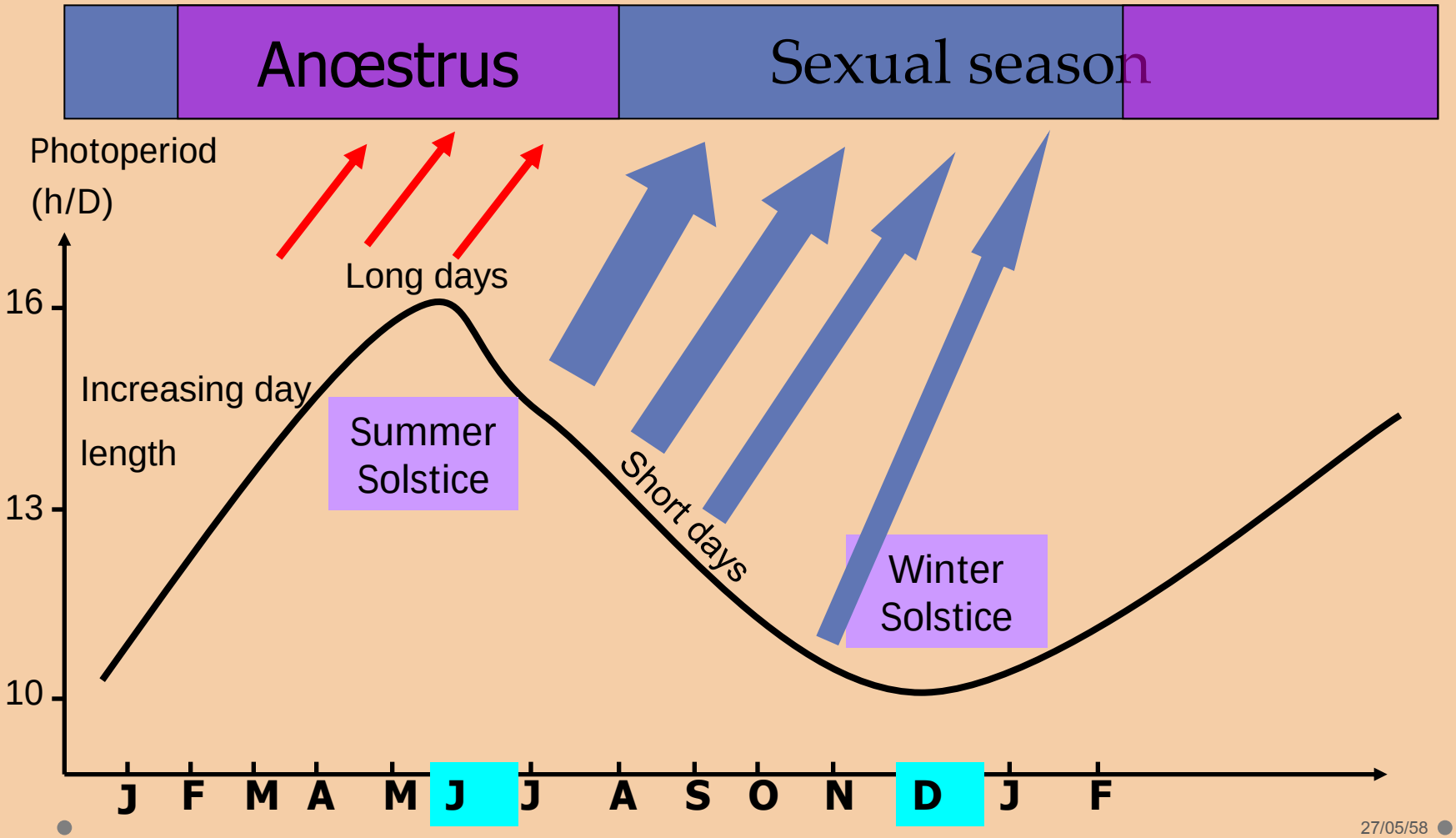
seasonally polyestrous

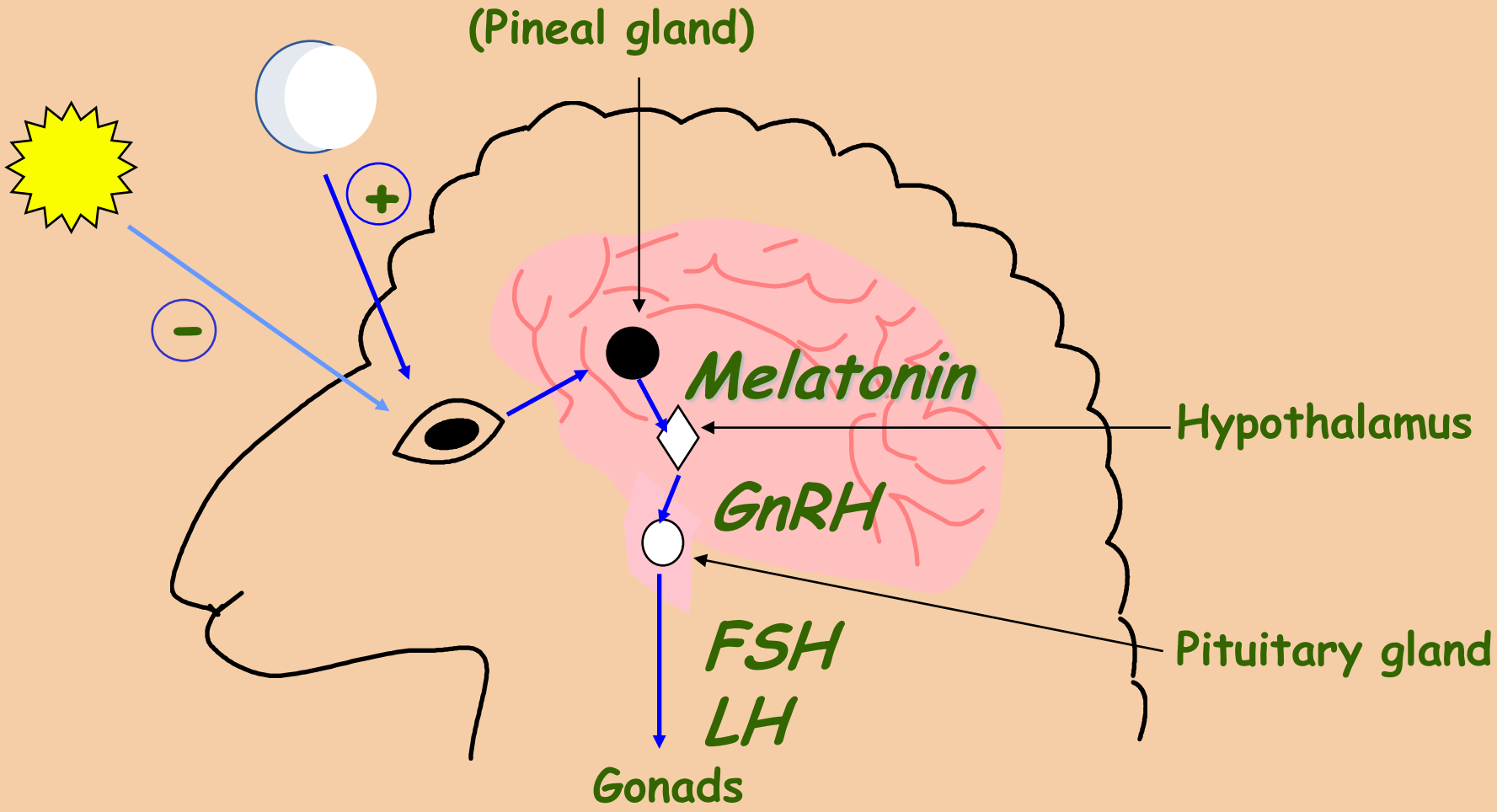
short- day breeders

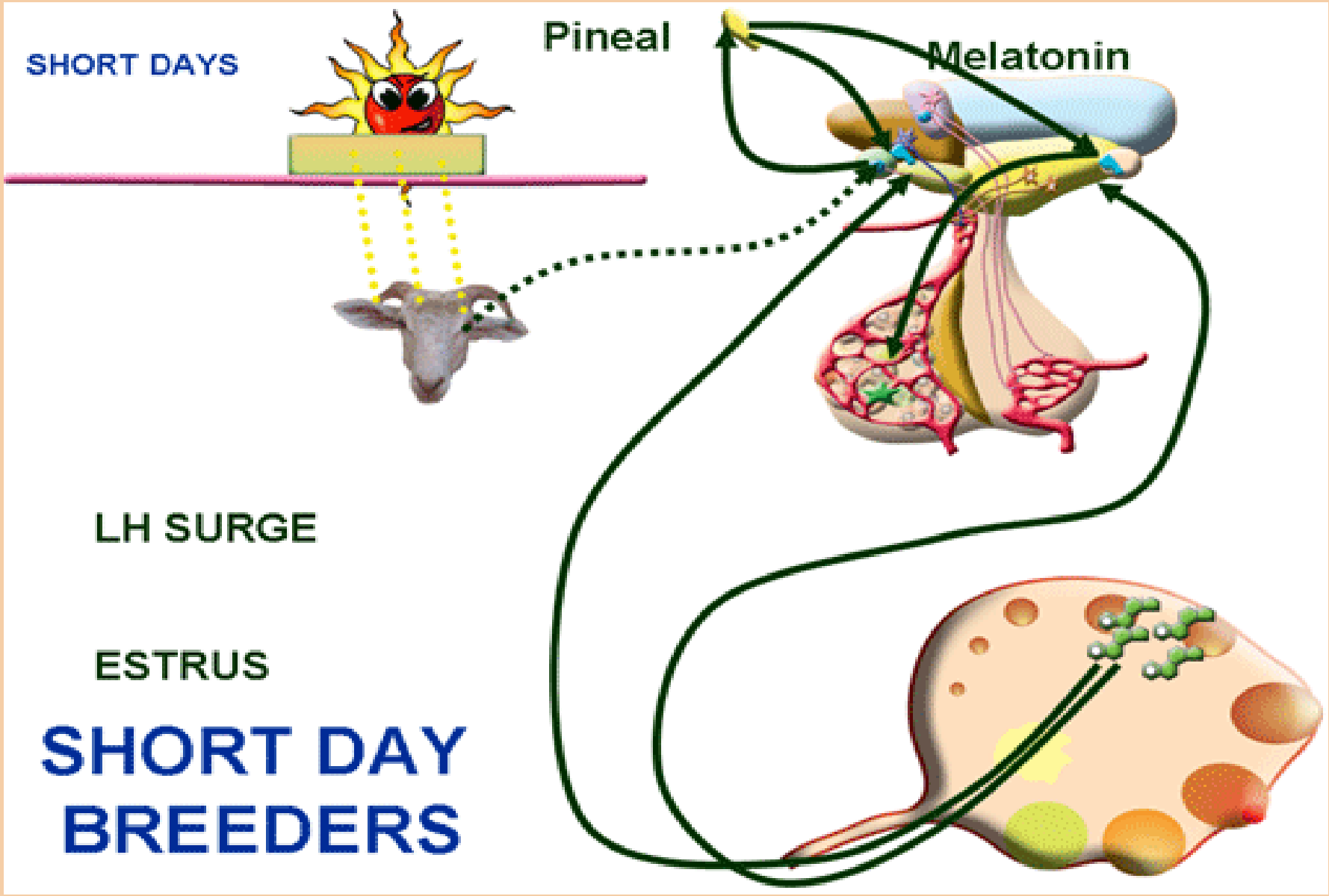
Reproduction in Farm Animals

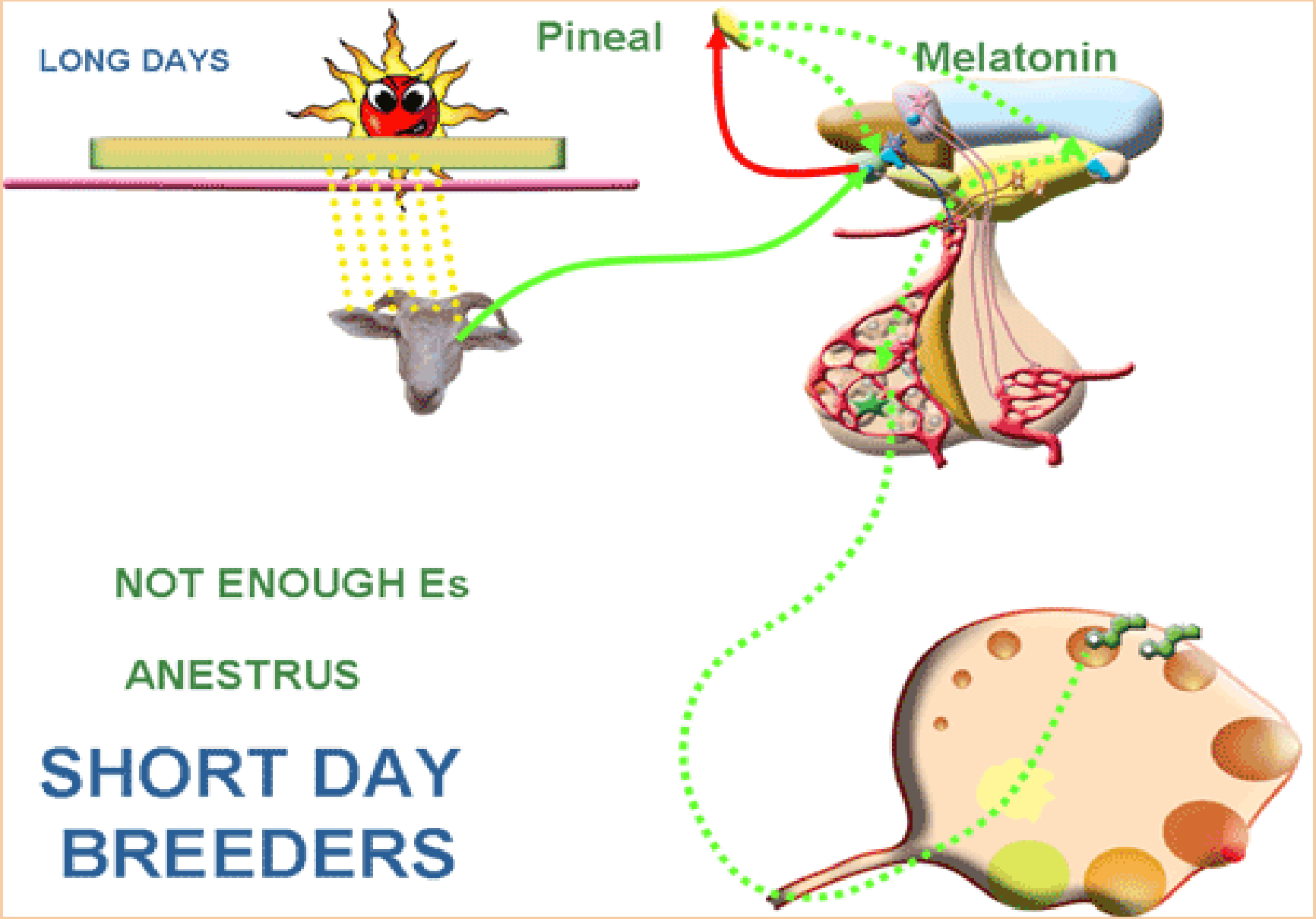


Involvement of Photoperiod




(Pineal gland)
+
−
Melatonin
Hypothalamus
GnRH
FSH
LH
Pituitary gland
Gonads

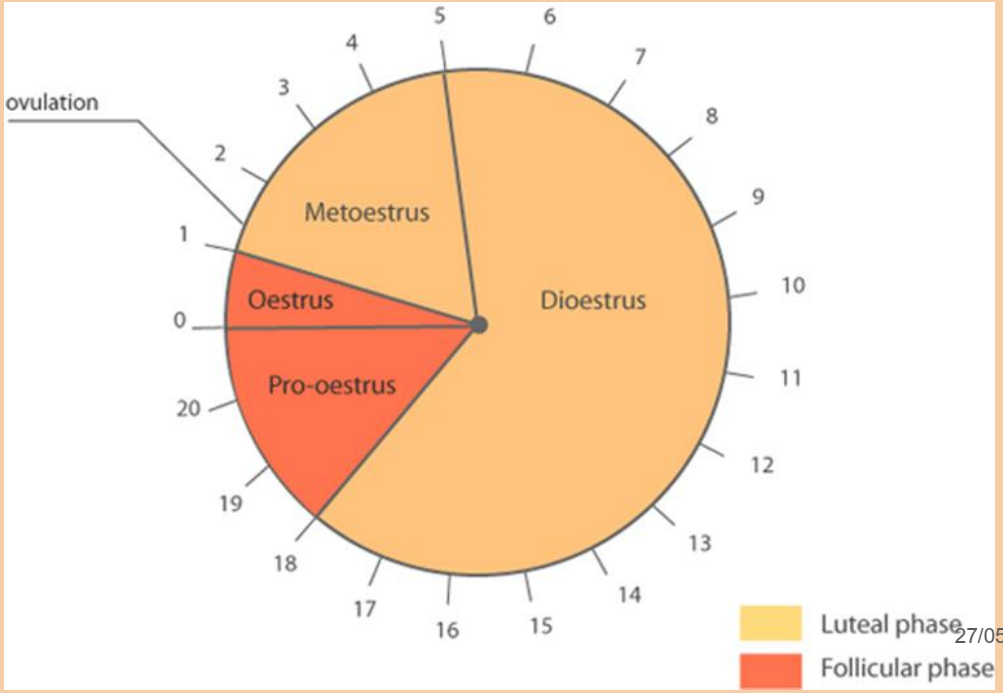

SHORT DAYS
Pineal
Melatonin
LH SURGE
ESTRUS
SHORT DAY
BREEDERS


LONG DAYS
Pineal
Melatonin
NOT ENOUGH Es
ANESTRUS
SHORT DAY BREEDERS

Divided into phases

- follicular phase 3-4 day
- luteal phase 14-15 day

(Jordan, 2005)



Duration of estrus

- varies with age, breed
- presence of the male
- 18 and 72 hours (36 hours) (Hashemi et al, 2006)

- 30 ชม. (บุญเสริม, 2547)

Ovulation time

- 14 h. after LH surge or 24 h. after beginning of estrus (Pierson et al., 2001)
- Near the end of estrus about 24 to 27 hours after onset of estrus (Bearden and Fuquay, 1984)

Estrus in the ewe

- Seek and walk to a ram
- Tail- wagging
- Nuzzle ram scrotum
- Stand to be mounted
- **Standing heat**
- If no ram or an inexperienced one is present estrus can remain undetected

(Bearden and Fuquay, 1984)

Why synchronize ?

- Group femmale for parturation (claving interval)
- Shotern breeding seasone
- Reduce estrus detection

Improvement of fertility

Control over the events of the oestrous cycle

Breeding season

Synchronisation

Anoestrous season

Induction

Synchronisation

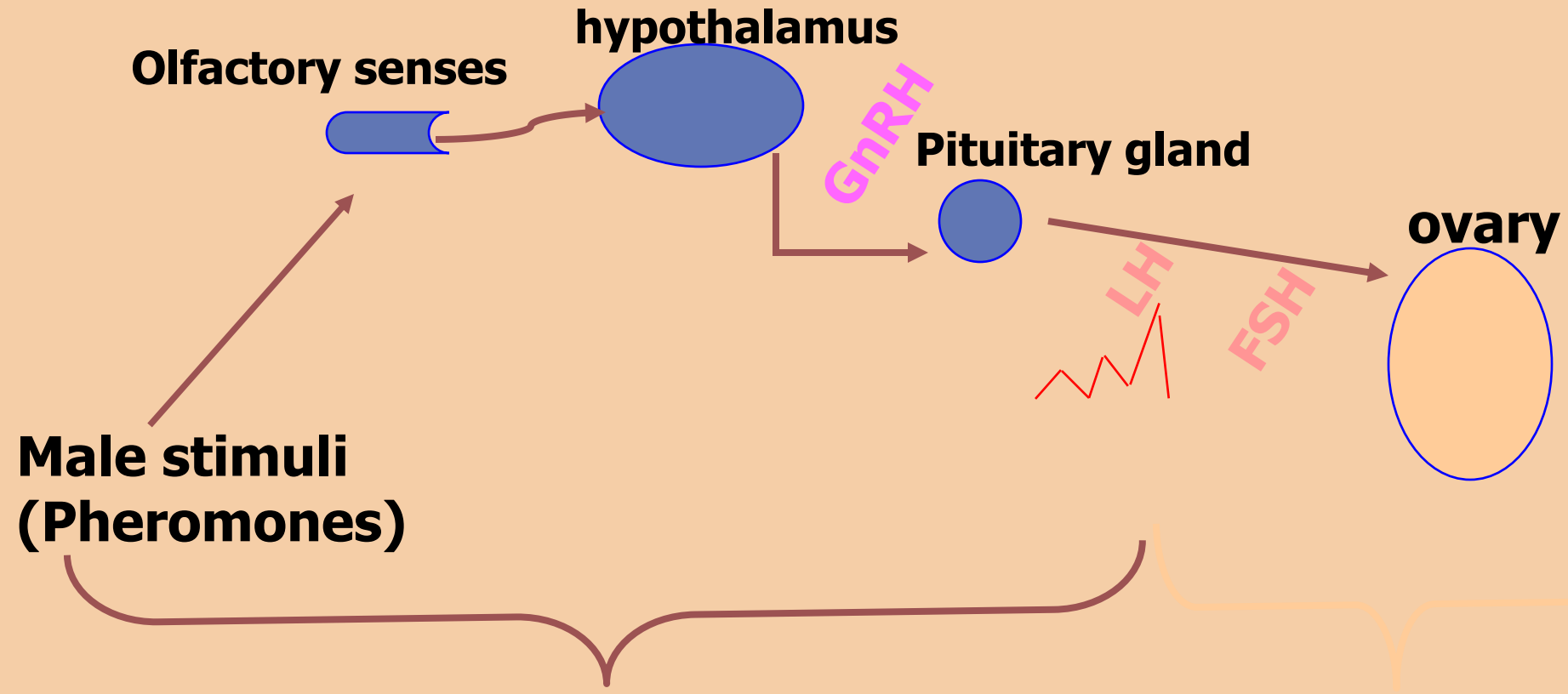
Synchronization method

- Introduction of Rams
- Melatonin
- Shortern of luteal phase
- Extend of luteal phase

Introduction of Rams

- **Isolated with rams before the start of normal breeding season, introduction of rams to ewes inducing ovulation “Ram effect” (Jordan,2005)**
- **Including pheromone,sight, sound, and smell**
- **responsible pheromones are present ram hair, but not in urine (Walkden-Brown et al., 1993b)**
- **GnRH release from hypothalamus**
- **increase LH and causing onset follicular phase and E2 causing onset follicular phase**
- **After introduction of ram LH surge within 6 to 8 h.**

Natural method: The «male effect»



continuous

Onset of estrous

D 0

32.9±1.6 h.

14 days

Insert FGA

- Remove FGA
- PMSG

intermittent

Onset of estrous

D 0

45.3±4.4 h.

14 days

Insert FGA

- Remove FGA
- PMSG

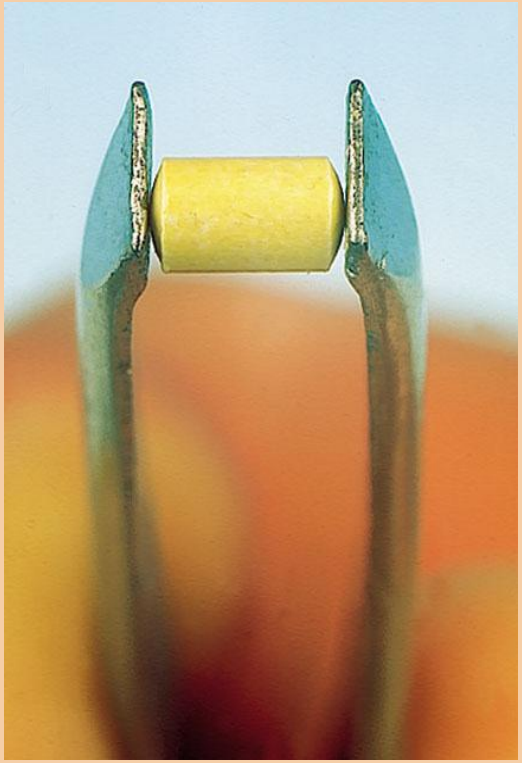
Romano et al. (2001)

- First ovulation is usually silent and low fertility
- The response to the male effect is influenced by such factors as sexual aggressiveness of the ram (Perkins and Fitzgerald, 1994)

Melatonin

- darkness hormone
- secreted from pineal gland
- secretion increase when the day length becomes shorter
- effect on hypothalamus and secretion of the gonadotropin hormone
- when using 2 or 10 mg or implant for 40 days that enhanced reproductive performance which synchronized estrus was increased and lambing in mature ewes (Stellflug et al, 1988)

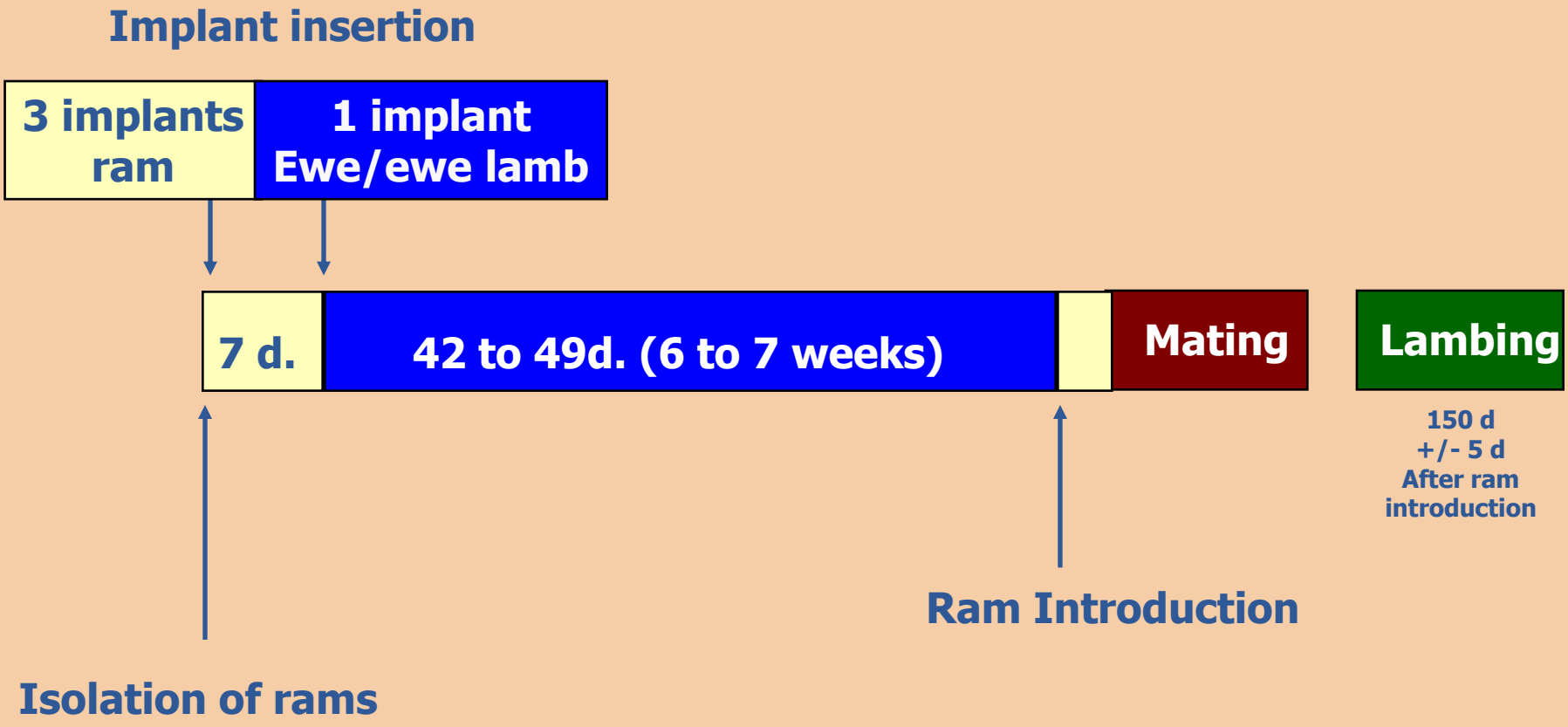
MELATONIN



Regulin®/Melovine®

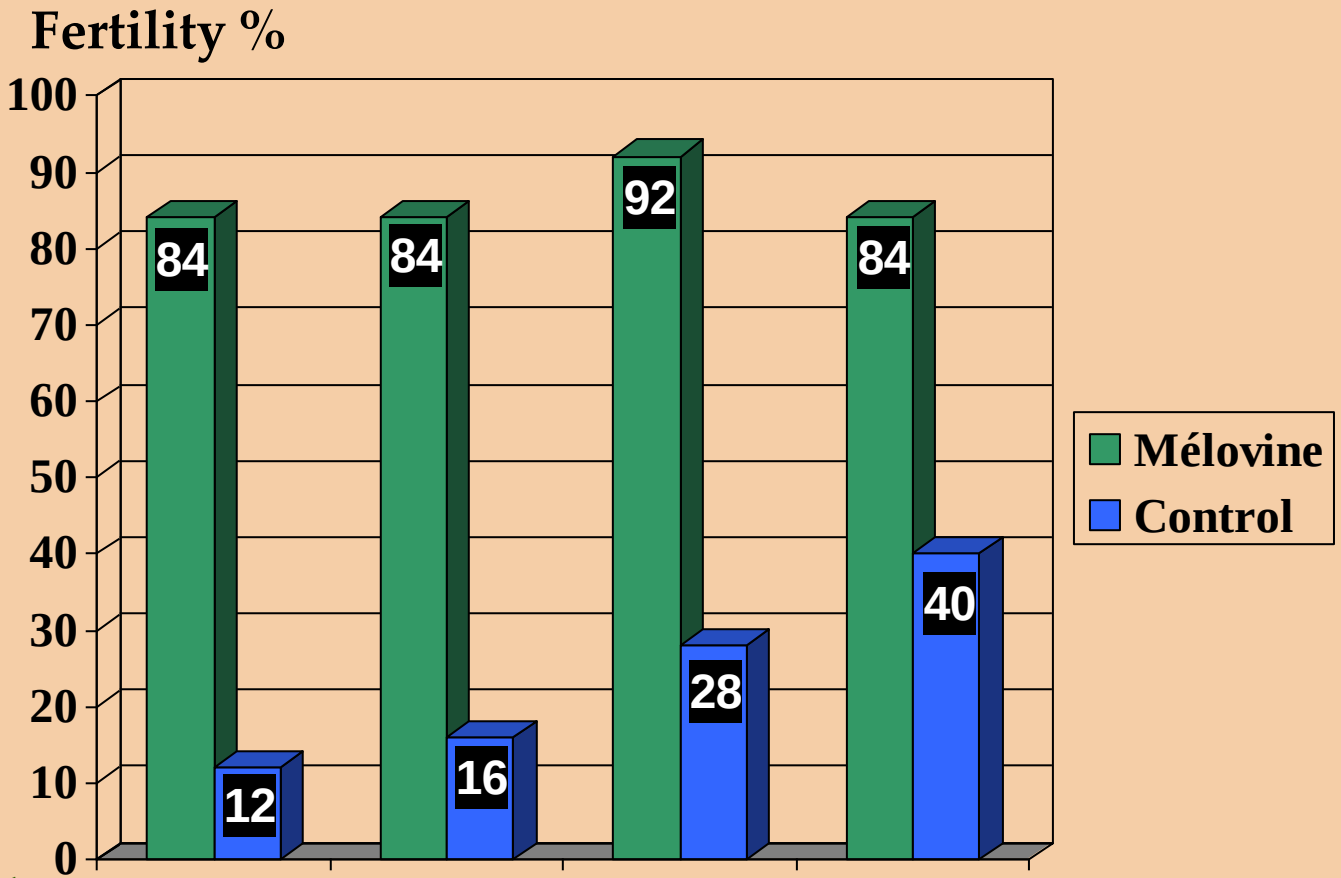
- Each implant contains 18 mg melatonin
- moves the reproductive peak from autumn to spring
- Use by subcutaneous implantation only
- Administer one implant to each ewe 30 to 40 Days before joining rams with the ewes
- CEVA Animal Health Ltd

Melatonin Protocol



Mélovine (CEVA®)

- *Awassi breed- Syria*

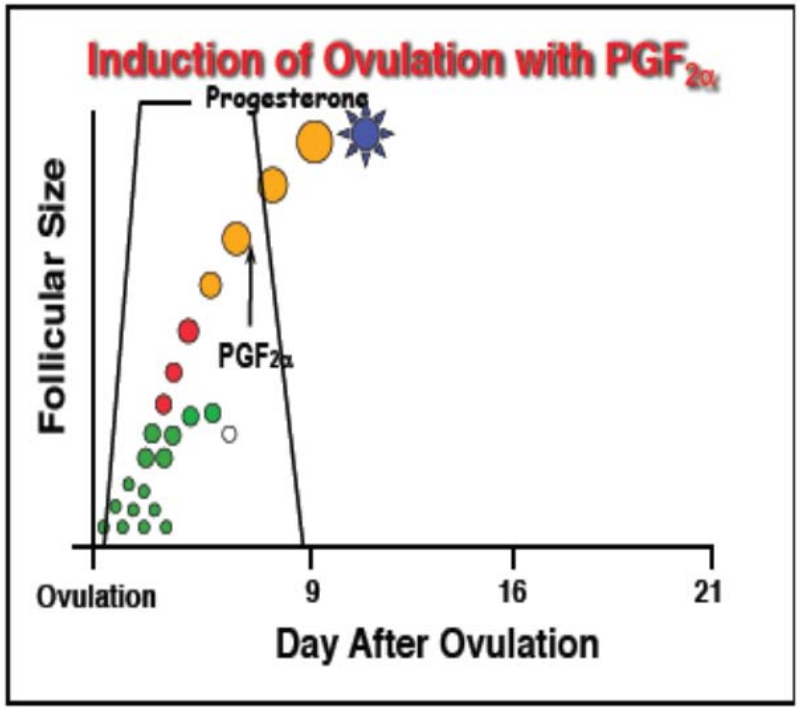


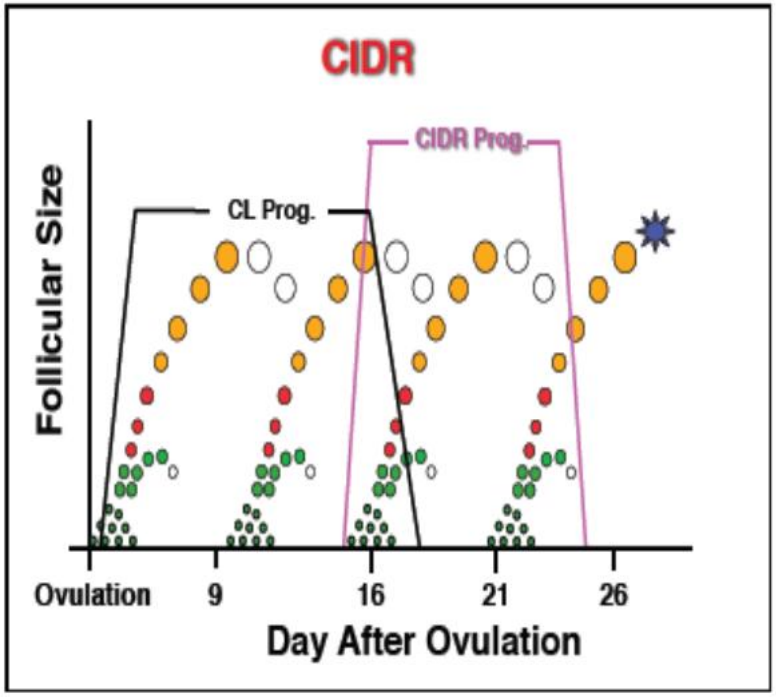
Implant in :	26 March	9 April	23 April	7 May
Mating :	May	End May June	mid June mid July	end June July

Principles of oestrus synchronization

1. Shortening life span of CL- PGF2ə/analogue

2. Prolonging luteal phase- Progesterone/progestagen





Comparison of prostaglandin & progesterone based synchronization

	Progesterone/its analogue	Prostaglandin/its analogue
Advantage	Induces cyclicity	Cheaper
	More efficacy synchronize	Easy to apply
	Does not induce abortion	Treat luteal cyst
disavantage	Expensive	Effective only in cycling
	Complicated application procedures	Effective from 4 to 14 days of estrous cycle (matured CL)
		Induces abortion if pregnant ewe is injected by mistake

Shortern of luteal phase

- Prostaglandin used synchronize estrus by the luteal phase through regression CL
- PGF2α used only during the breeding season
- Prostaglandin-based ES systems control the estrous cycle
- The most use progesterone impregnated intravaginal for 7 or 19 days following by a single PGF2α injection (Ataman and Aköz, 2006)

Shortern of luteal phase

- **Another method 2 injection of PGF2α at 11days interval, this method can be used only during breeding season (Ataman and Aköz, 2006)**
- **Commonly used products are**
  - **Naturally prostaglandin**
  - **Prostaglandin analogue**

Prostaglandin ($PGF_{2\alpha}$)

I: intramuscular injection of 125 mg of Cloprosterol (Estrumate®)

Estrus synchronisation with Ovsynch Protocol

G

GnRH (Receptal /Fertagyl 2.5 ml)

P

$PGF_{2\alpha}$ (Estrumate 2 ml)

G

GnRH (Receptal /Fertagyl 2.5 ml)

Fixed time AI

Ovulate the dominant follicle
Intiate the new follicular wave

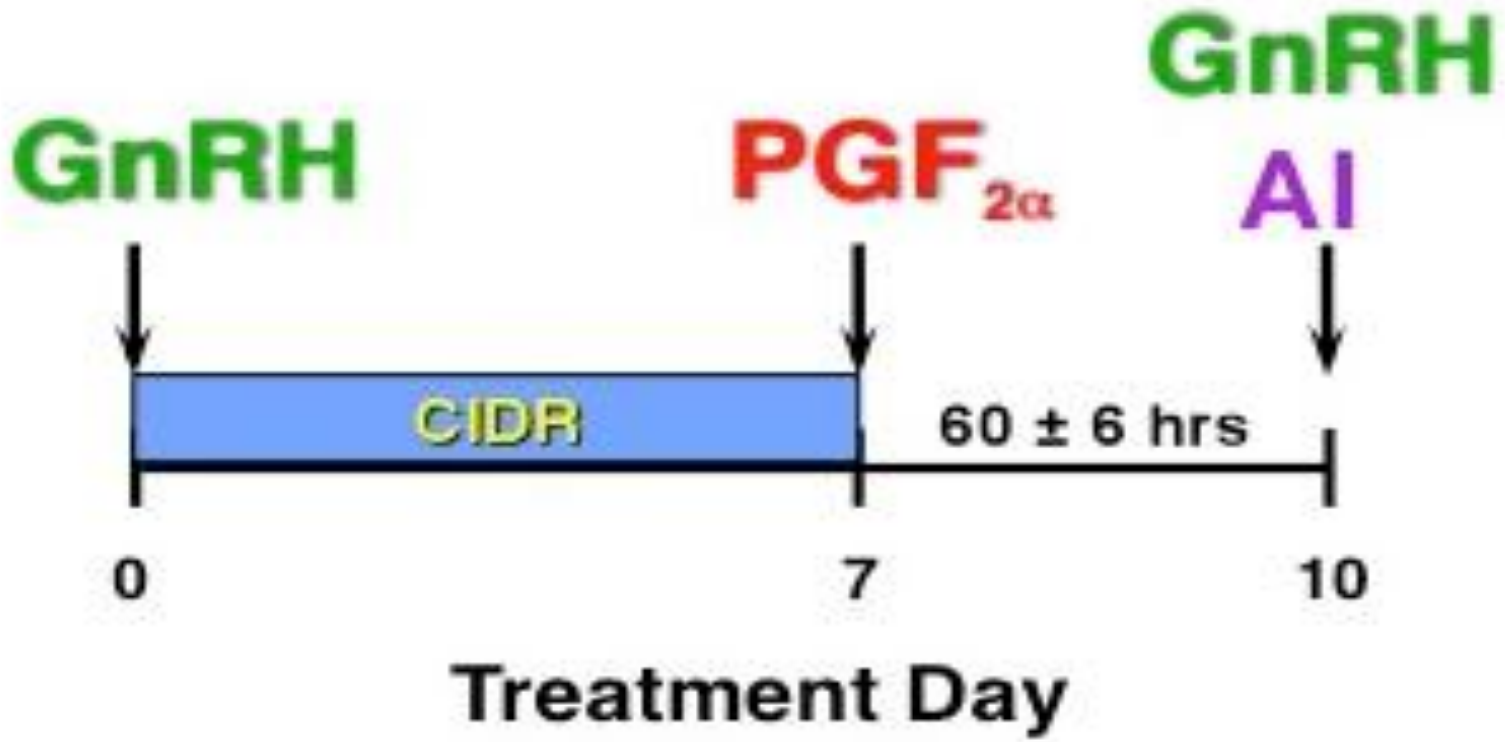
Induce luteolysis

Induce ovulation of new dominant follicle

Synchronisation of estrus

Synchronisation of ovulation

Co-Synch + CIDR



LutaLyse®

- naturally occurring prostaglandin F2 alpha
- sterile solution Dinoprost tromethamine 5mg/ml for injection
- Recommended Use 5mg/ewe
- Zoetis;Pharmacia &Upjohn, Spain

Estrumate®

- synthetic prostaglandin analogue
- Equivalent to 250 µg cloprostenol/ml
- Recommended Use 125µg/ewe
- Merck Animal Health; New Zealand

Prostaglandin

- The mean onset time was 46 to 48 h and LH surge at 62 to 64 h after injection
- No difference of 62.5 and 125 µg cloprostenol in the onset and duration of estrus and injected once between d 8 and 15 of the estrous cycle (Romano, 1998a)
- Boer goats in nonbreeding season
  - estrous response was lower ($P < .01$) in double PGF injection (13 to 20%)
  - sponges and sponges plus PGF (87 to 100%)(Greyling and Van Niekerk, 1991

Prostaglandin

- No difference was observed in cyclic Menze ewes in the estrus response (83%) following PGF (2.5 mg, 12 d apart) and sponge (FGA, 40 mg for 12 d) treatment
- but PGF-treated ewes exhibited estrus ($P < .05$) earlier (–6 h) than sponge-treated ewes (Mutiga and Mukasa-Mugerwa, 1992)
- onset of estrus after PGF (10 mg, 11 d apart) compared to sponge (MAP, 60 mg for 14) treatment in West African Dwarf sheep (41.2 vs 77.7 h; $P < .05$) (Oyediji et al., 1990)

Prostaglandin

- **Beck et al. (1993) compared**

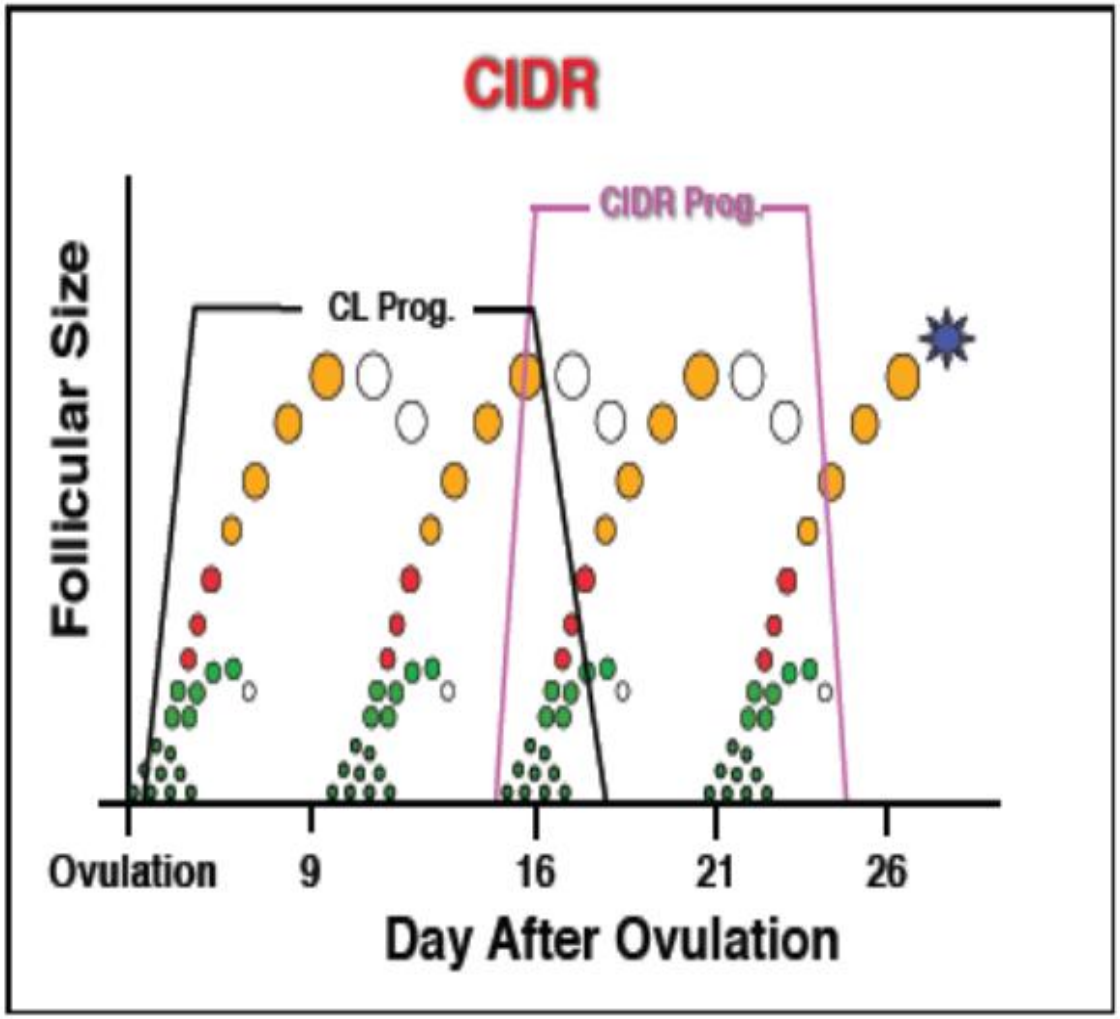
  T1 double injection system (125 µg cloprostenol 11 d apart)

  T2 single injection

  T3 combination of short-term progestagen treatment (MAP, 5 d) with a cloprostenol injection at sponge removal in ewes

- **They found**
  - **a 100% estrus response in the double injection and MAP-PGF combination treatment**
  - **whereas estrus response was reduced in the single injection group (52.9%; $P < .05$).**

Extend of luteal phase



Use of Exogenous Progesterone/Progestagens

- Exogenous progesterone/progestagens extend luteal phase
- the CL regresses naturally during the period when exogenous source is applied
- The exogenous source continues to exert a negative feedback on FSH and LH secretion, even after CL regression
- When external source is later withdrawn, follicular growth starts simultaneously in all treated females

Routes of administration of progesterone/progestagens

- **Oral administration**
- **skin implants**
- **Intravaginal treatments**

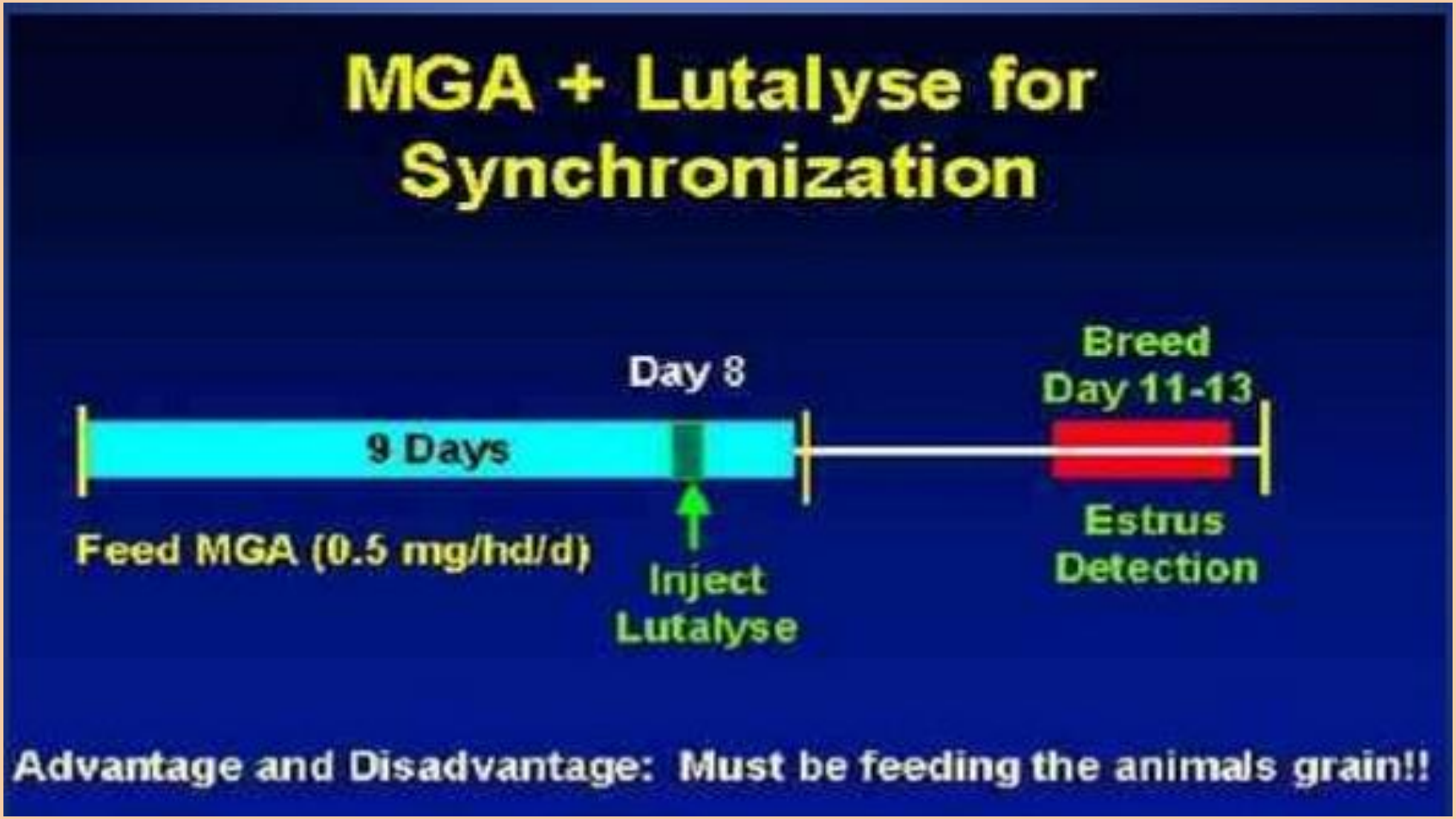
The oral administration

- Melengestrol acetate (MGA), an orally active synthetic progestagen
- twice daily feeding of 0.125 mg MGA for an 8-day period could induce an out-of-season synchronized oestrus in ewes.

disadvantate:

- time and labour costs involved in oral dosing
- difficulty to succeed a smooth and input of progestagen
- Less practical and predictable result

Feed MGA Shot term



Feed MGA Long term

Implant treatments

- Subcutaneous implant of norgestomet used
- About 1cm implant contains 1.2 or 3mg of norgestmet is inserted for 13 days.
- Mean time of onset of oestrus after removal of implant is 26 to 30 hrs

Implant in sheep

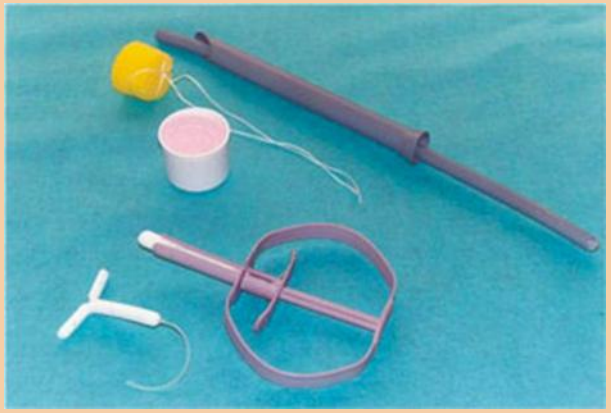
Intravaginal administration

The treatment of choice for oestrus synchronization in sheep (in all seasons).

- Progestagen impregnated sponges used
- Inserted over periods of 12 to14 days
- Used in conjunction with PMSG

Intravaginal administration…

- **FGA (Fluorogestone acetate)**
  - **marketed as Chronogest® or Cronolone®. (30-45 mg),**
  - **widely used either in conjunction with PMSG, FSH or PGF2ə**



Animal	FGA dose	Duration of insertion (days)	PMSG (i/m or s/c dose) dose/timing
Breeding Season			
Dry Ewe	40mg	14	400iu-600iu At sponge removal
Lactating Ewe	30mg	12	400iu-600iu At sponge removal
Maiden Ewe	40mg*	14	400iu-600iu At sponge removal
Doe	45mg*	17-21	400iu At sponge removal
Non Breedind Season			
Dry Ewe	30mg	12	400iu-600iu At sponge removal
Lactating Ewe	30mg	12	400iu-600iu At sponge removal
Maiden Ewe	40mg*	14	400iu-600iu At sponge removal
Doe	45mg*	17-21	600iu 2 days before sponge removal

Animal health product

http://pharmplex.com.au/Products/fluorogestone_acetate_sponges.htm

Intravaginal administration…

- **MAP (medroxyprogesterone acetate)**
  - **6-methyl-17-acetoxyprogesterone**
  - **marketed as Sincrogest Esponjas™ (Laboratorios Ovejero, Spain)**
  - **Contain 60 mg of the progesterone analogue**
  - **The same effect as FGA**

Medroxyprogesterone acetate (MAP)

- Medroxyprogesterone acetate, 60 mg
- Polyurethane sponge
- used with the PMSG
- Insert 12 - 14 days
- removed after 12 - 14 days and injection of 400-600 UI of PMSG

SINCROGEST SPONGES

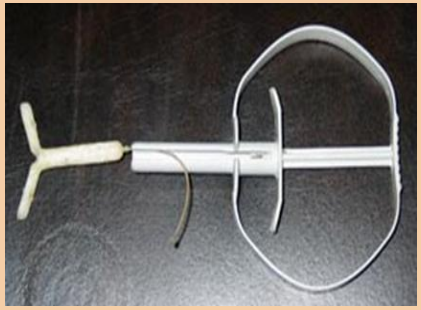
Sincrogest Esponjas™,

Laboratorios Ovejero, Spain

http://www.labovejero.com

Intravaginal administration…

- **CIDR (Controlled Internal Drug Releasing)**



- **dispenser developed in New Zealand.**
- **constructed from a natural progesterone impregnated medical silicone elastomer.**

CIDR-G

http://www.zoetis.co.nz

Intravaginal administration…

Advantage

- natural progesterone
- aesthetically more pleasant to handle
- Less vaginal discharge

Disadvantage

- higher incidence of loss (13.5%) compared to sponges (6.7%)
- more expensive than the progestagen sponges

Controlled internal drug release(CIDR)

- Progesterone intravaginal insert for controlled breeding in sheep and goats
- Contains 0.3g progesterone in an inert silicone elastomer
  - Breeding season insert the device for 12–14 days.
  - Outside breeding season inserted for 7–12 days with PMSG administered at the time of device removal

FGA , MAP and CIDR

- efficacy on estrous response, onset of induced estrus, estrous duration and fertility
- found that
  - no significant difference in estrus response and fertility between treatments Romano, 2004

Intravaginal progestagen

- **Intravaginal sponges are usually inserted 9 to 19 d and used PMSG injected at time of sponge removal or 48 h prior to sponge removal**
- **Exhibited estrus within 24 to 48 h after removal**

(Wildeus, 2000)

Decreased periods

- P4 will be higher during the first 2days of insertion sponge in vagina
- decreases gradually with time during the remaining the sponge (Husein et al., 1998)
- removal in a 12-day treatment may not be maintain normal patterns of follicular growth (Gordon, 1975)

Decreased periods

- Decreased periods of progestagen in a 6-7 d may be maintain higher P4 levels of follicular growth and development
- Facilitate management
- Decress Vaginal discharge and infection, and increase fertility (Amer and Hazzaa, 2009; Kajaysri and Thammakarn, 2012)

MAP 40,50,60 mg

- For 14days,he found
  - The time of sponge removal to estrus onset in lower dose of progestagen exhibited an earlier estrus response Simonetti et al, 2000

Progesterone acetate in oil, CIDR and MAP

- **Used 20 mg progesterone acetate in oil every day for12 days, CIDR (0.3 g P4) for 12 days and 60mg MAP for 12 days and following injection 500 IU eCG, found**
  - **CIDR and MAP give higher effectiveness to estrus synchronization for ewes** Hashemi et al, 2006

6 Day treatment , FGA /PGF2/ eCG and CIDR /PGF2/eCG

- **Ewes in estrus**
  - **FGA 95.9% (70/73)**
  - **CIDR 93.2% (68/73)**
- **Ewes lambing**
  - **FGA 48.3% (70/145)**
  - **CIDR 51.4% (74/144)**

Fleisch et al,2012

Short- and long-term progestagen

- (FGA1)FGA-eCG-PGF2(**7d**) / (FGA2)FGA-eCG-PGF2(**12d**) / (GNRH)GnRH-FGA-eCG-PGF2(7d)

Parameters	Group FGA1	Group FGA2	Group GnRH
Estrous response (%)	88.8 (71/80)	92.5 (74/80)	96.3 (77/80)
Fertility rate (%)	87.3 (62/71)a	71.6(53/74)b	89.6 (69/77)a
birth rates (%)	51.6 (32/62)b	51.0 (27/53)b	71.0 (49/69)a

Karaca et al,2009

MAP 60mg/PMSG and 30mg/ PMSG

- progesterone (MAP 60mg, 30mg) and 300IU PMSG at withdrawal of sponge in two breeds, found
  - no different in the efficiency of synchronization in different breeds
  - but the onset of estrous in 30mg shorter than 60 mg the reason for the delayed time to
- incidence the estrus of 60mg MAP may be to more residual progesterone (Greyling and van der nest, 2000)

CIDR and MAP for 7 d and AI

Treatment 1	Estrus Onset (h.)		Estrus Duration (h.)		estrus	Pregnant(40d)
1. CIDR-G+PMSG+PG $F2_{\alpha}$	44^{a}	±6.00	22^{c}	±5.20	100 % (9/9)^{a}	11.11% (1/9)^{b}
2. MAP+PMSG+ $PGF2_{\alpha}$	54^{b}	±5.55	19.5^{c}	±5.32	88.89% (8/9)^{a}	0% (0/9)^{b}
Average	49	±5.76	20.75	±5.26	94.45% (17/18)	5.56(1/18)

CIDR and MAP for 7 d and Ram mating

Treatment 2	Estrus Onset (h.)		Estrus Duration (h.)		Estrous	Pregnant(40d)
1. CIDR-G+PMSG+PGF2$_\alpha$	54[a]	±18.06	15[b]	±10.33	75(9/12) [c]	41.66(5/12) [d]
2. MAP+PMSG+PGF2$_\alpha$	50[a]	±9.84	20.1[b]	±8.08	71.43(10/14) [c]	64.29(9/14) [d]
Average	52	±13.95	17.55	±9.21	73.22(19/26)	52.98(14/26)


Thank you