Theriogenology
(Andrology, Gynecology & Obstetrics)

Dr. Peyman Rahimi

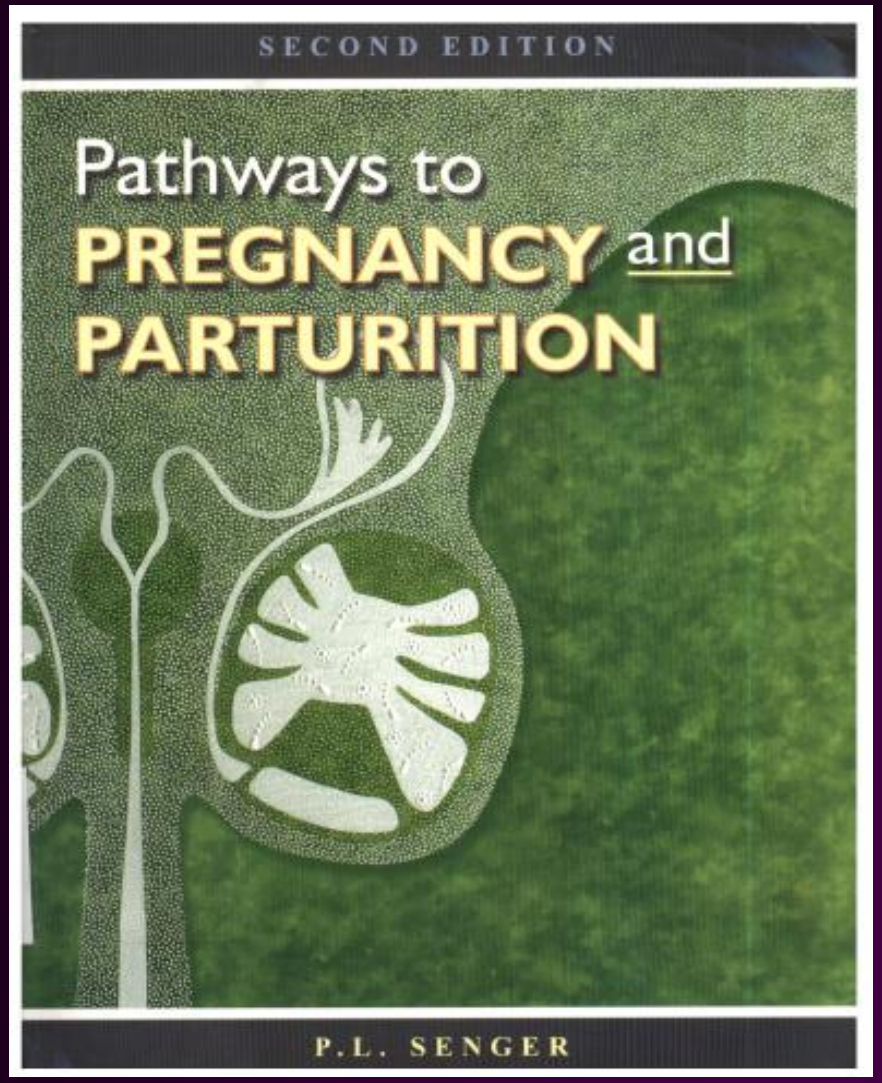
DVSc in Theriogenology

Department of Clinical Sciences, Razi University, Kermanshah, Iran

E-Mail: drp.rahimi@gmail.com

Text book

Chapters7, 8,9,10,12,13,14



Reproductive Cyclicity
Terminology and Basic Concepts

Reproductive cyclicity

- Estrous Cycle
- Menstrual Cycle

Estrous Cycle

- *After puberty, the female enters a period of reproductive cyclicity that continues throughout most of her life.*

- *Estrous cycles consist of a series of predictable and reproductive events beginning at estrus (heat) and ending at the subsequent estrus.*

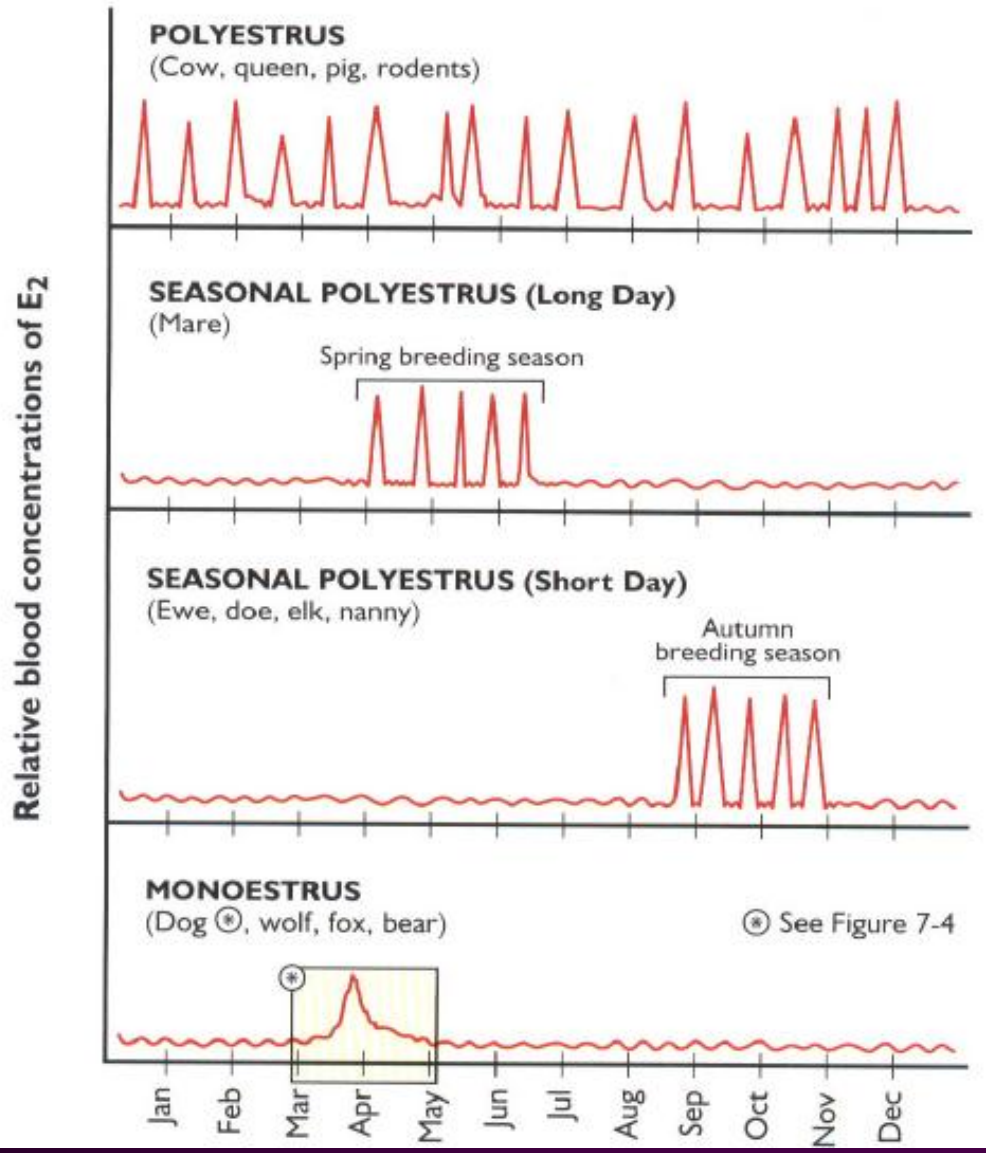
ESTRUS is a noun.
"The cow is displaying estrus."

ESTROUS is an adjective.
"The length of the estrous cycle in the pig is 21 days."

The three types of cyclicity are:

- *polyestrus*
- *seasonally polyestrus*
- *monoestrus*

Figure 7-1. Types of Estrous Cycles as Reflected by Annual Estradiol (E_2) Profiles



The Estrous Cycle Consists of Two Major Phase:

- Follicular Phase:

from the regression of corpora lutea to ovulation(%20 of the estrous cycle)

- Luteal Phase:

from ovulation until corpora lutea regression (%80 of the estrous cycle)

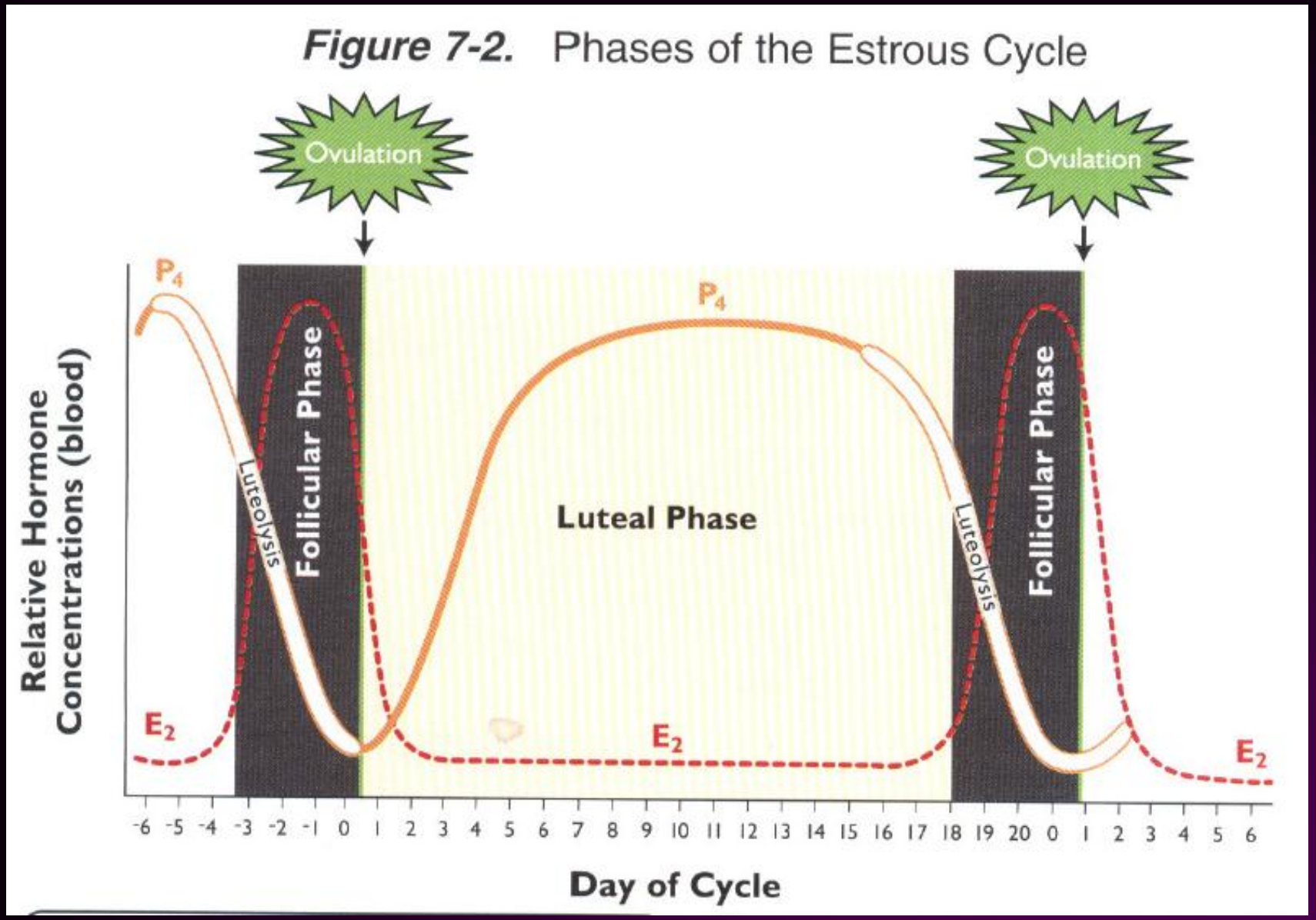


Figure 7-2. Phases of the Estrous Cycle
Ovulation
Ovulation
P4
P4
Follicular Phase
Luteolysis
Luteal Phase
Luteolysis
Follicular Phase
E2
E2
E2
Relative Hormone Concentrations (blood)
-6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 0 1 2 3 4 5 6
Day of Cycle

During the follicular phase:

- *follicles = the dominant ovarian structure*
- *estrogen (produced by follicles) = the dominant hormone*

During the luteal phase:

- *corpora lutea = the dominant ovarian structures*
- *progesterone (produced by corpora lutea) = the dominant hormone*

Follicular phase = Proestrus + Estrus

Luteal phase = Metestrus + Diestrus

Proestrus = Formation of ovulatory follicles + E_2 secretion

Estrus = Sexual receptivity + peak E_2 secretion

Metestrus = CL formation + beginning of P_4 secretion

Diestrus = Sustained luteal secretion of P_4

Figure 7-3. Stages of the Estrous Cycle

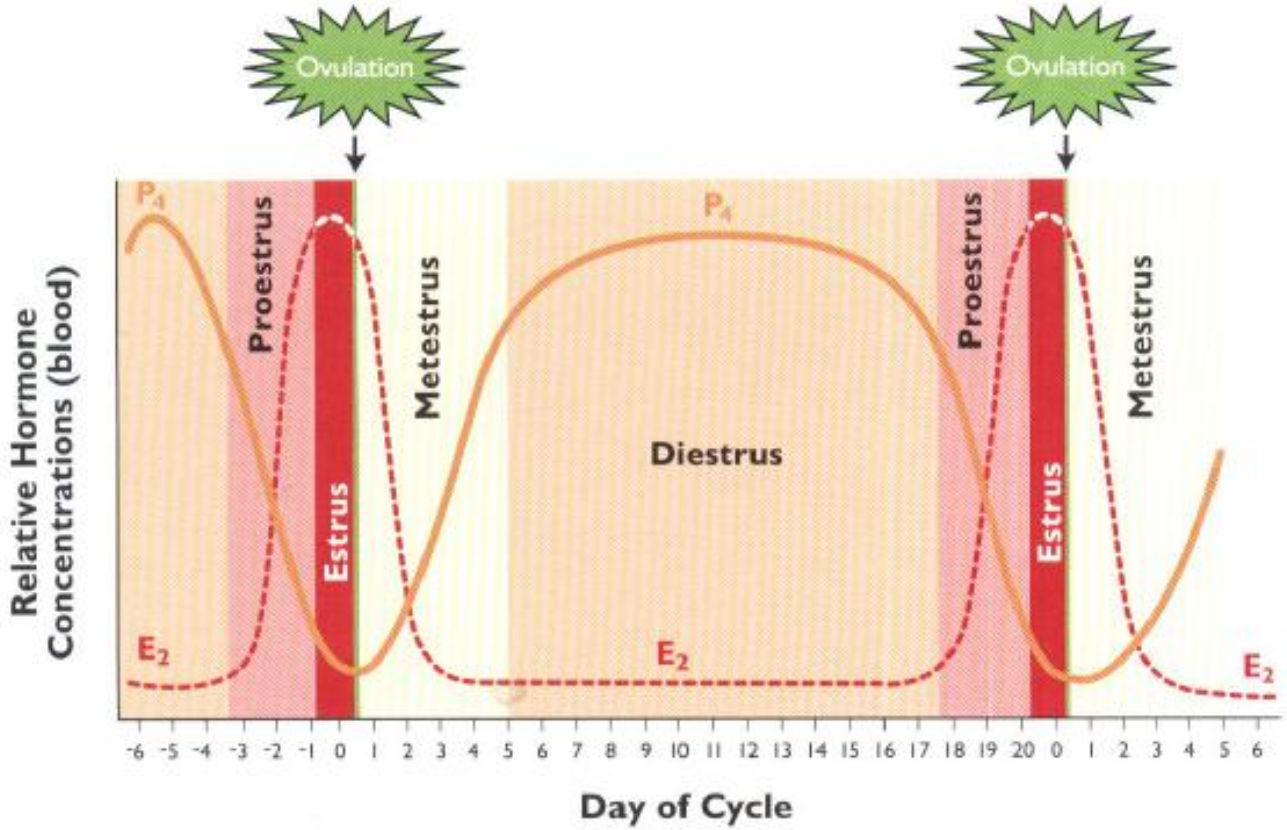
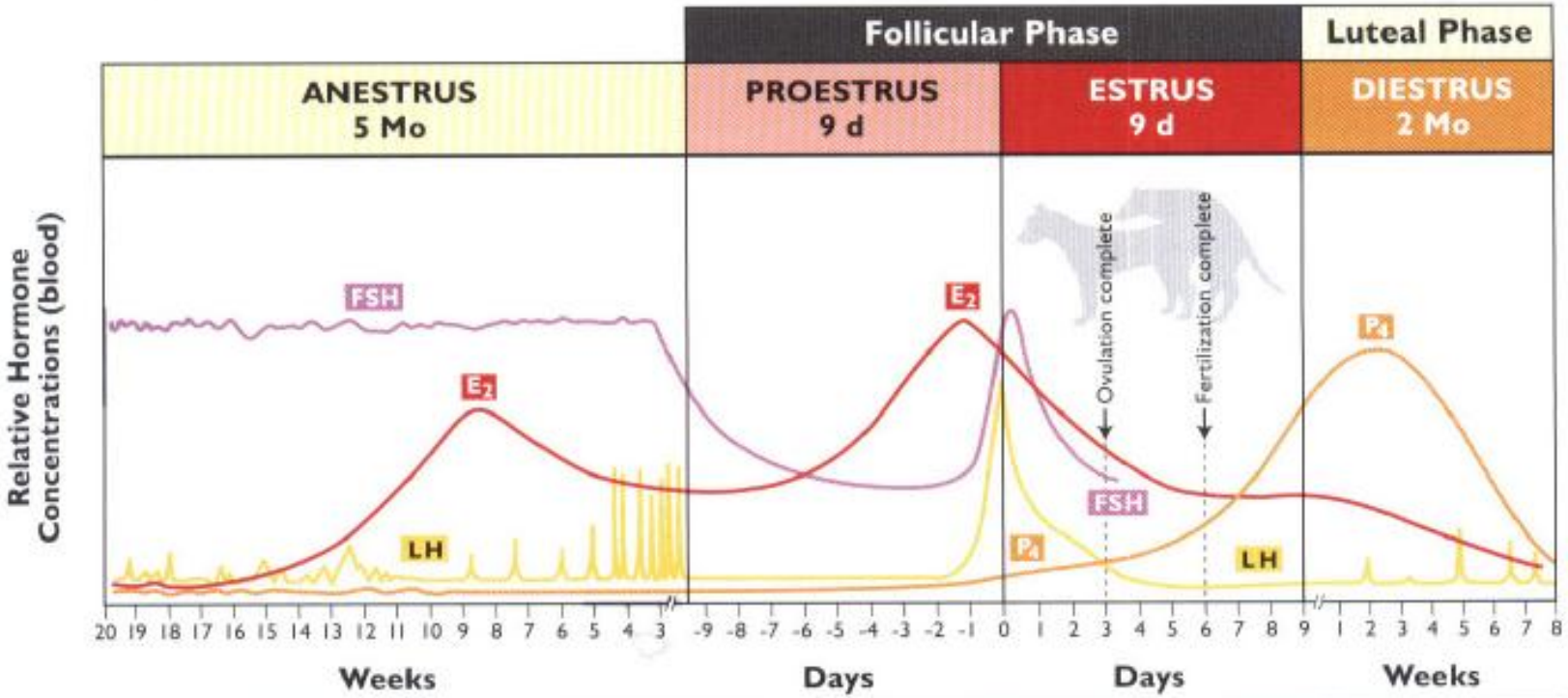


Table 7-1. Characteristics of Estrous Cycles in Domestic Animals

Species	Classification	Length of Estrous Cycle		Duration of Estrus		Time From Onset of Estrus to Ovulation	Time From LH Surge to Ovulation
		Mean	Range	Mean	Range		
Alpaca	Polyestrus	15d	(11-18d)	5d	(4-5d)	Induced Ovulator	26-36h
Bitch	Monoestrus	6 mo	(3-9 mo)	9d	(4-21d)	4-24d	2-3d
Cow	Polyestrus	21d	(17 - 24d)	15h	(6 - 24h)	24 - 32h	28h
Ewe	Seasonally polyestrus (Short Day)	17d	(13 - 19d)	30h	(18 - 48h)	24 - 30h	26h
Llama	Polyestrus	10d	(8-12d)	5d	(4-5d)	Induced Ovulator	24-36h
Mare	Seasonally polyestrus (Long Day)	21d	(15 - 26d)	7d	(2 - 12d)	5d	2d
Queen	Polyestrus	17d	(4-30d)	9d	(2-19d)	Induced Ovulator	30-40h
Sow	Polyestrus	21d	(17 - 25d)	50h	(12 - 96h)	36 - 44h	40h

Figure 7-4. The Annual Reproductive Cycle of the Bitch

(Modified from Johnston, Root Kustritz and Olson. 2001. *Canine and Feline Theriogenology*)



Anestrus

A period of reproductive quiescence. This long anestrus period is responsible for a cyclic profile of three cycles in two years.

Proestrus

Proestrus begins with the appearance of a blood-tinged vaginal discharge and by vaginal swelling. It ends when the bitch accepts the male for mating. The ovaries contain large follicles at the onset of proestrus. Estradiol gradually increases and peaks slightly before the onset of estrus.

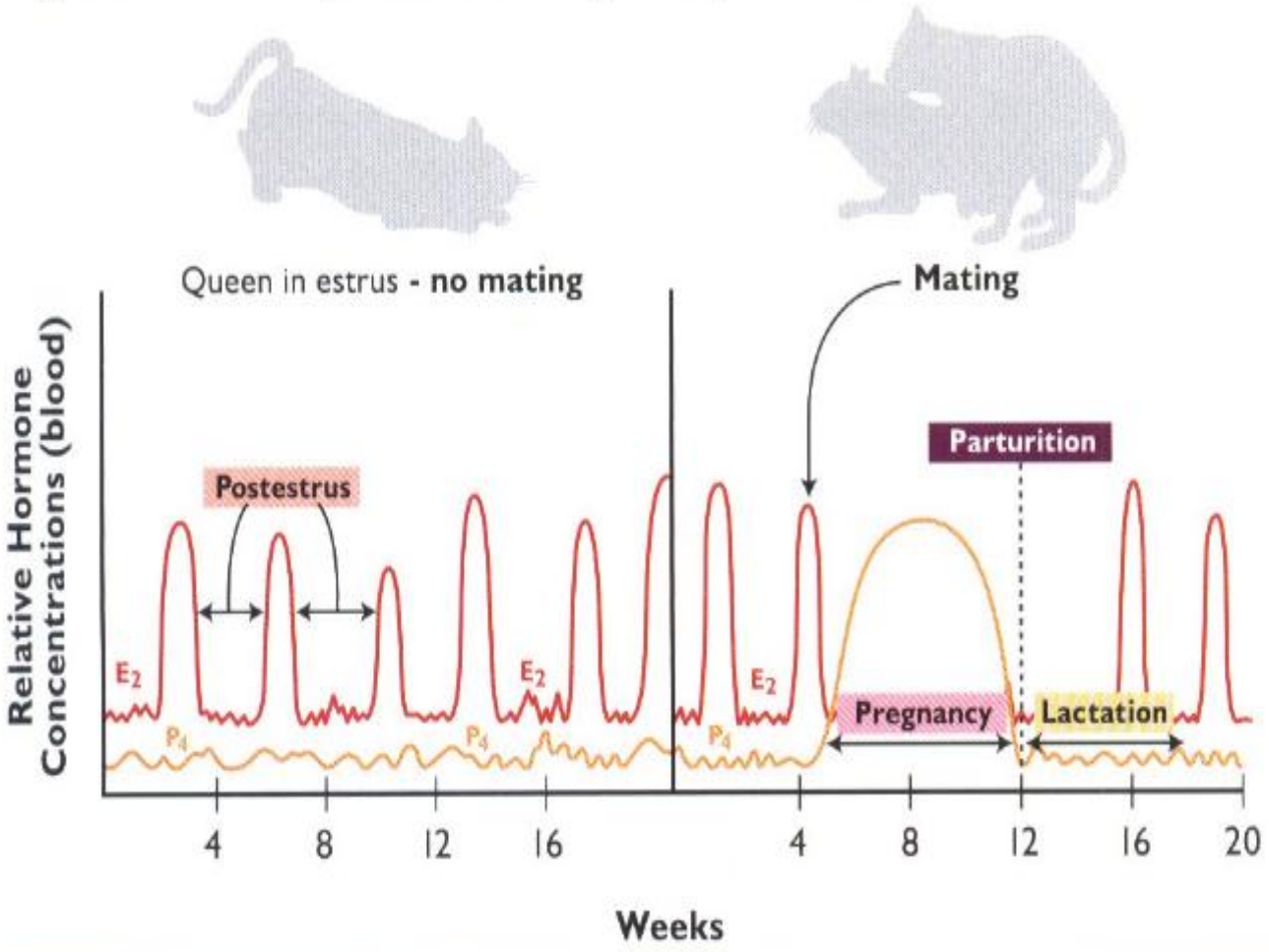
Estrus

Shortly after peak estradiol, behavioral estrus begins. Both LH and FSH peak in early estrus. Ovulation is completed at about the third day of estrus and fertilization is completed at about the sixth day. Progesterone increases during the latter part of estrus signifying luteinization.

Diestrus

Both pregnant and open bitches are considered to be in diestrus. Pregnancy status does not alter the length of diestrus. Progesterone peaks at about 15 days then decreases gradually. Bitches that do not become pregnant are often considered to be pseudopregnant.

Figure 7-5. Reproductive Cyclicity Profile of Queens With and Without Copulation



When mating occurs during estrus, ovulation is induced, fertilization occurs and pregnancy takes place. After ovulation corpora lutea are formed causing a marked elevation in progesterone. After a 60 day gestation period, parturition occurs and lactation ensues. Lactational anestrus does not occur in the cat because she will come into estrus while she is lactating.

A queen enters estrus (about 9 days) every 17 days. If copulation does not occur, the queen enters a postestrus phase and comes into estrus a few days later. Since the queen is an induced ovulator, when mating does not occur, ovulation does not occur and a CL is not formed.

Anestrus

Anestrus is a condition when the female does not exhibit regular estrous cycles. During anestrus the ovaries are relatively inactive and neither ovulatory follicles nor functional corpora lutea are present. Anestrus is the result of insufficient GnRH release from the hypothalamus to stimulate and maintain gonadotropin secretion.

It is important to distinguish between **true anestrus** caused by insufficient hormonal stimuli and **apparent anestrus** caused by failure to detect estrus

Anestrus can be caused by:

- *Pregnancy*
- *Lactation (mare & alpaca are exception)*
- *Presence of offspring*
- *Environmental Conditions* (*Stress, Nutrition*)
- *Pathological Condition* (*Uterine infection, Persistent cl,...*)
- *Season* (*In some species*)

Figure 7-6. Influence of Estradiol (E_2) and Progesterone (P_4) Upon the Brain and Subsequent Behavioral Estrus in the Cow and Ewe

Following seasonal anestrus in the ewe or pregnancy in the cow, the ovary develops a follicle(s) that will often ovulate without an accompanying behavioral estrus ("silent" ovulation).

The corpus luteum produced from the ovulatory follicle from the silent ovulation secretes progesterone (P_4) that "primes" the brain.

The priming of the brain by P_4 enables estradiol (E_2) secreted by the next ovulatory follicle to elicit a full behavioral estrus.

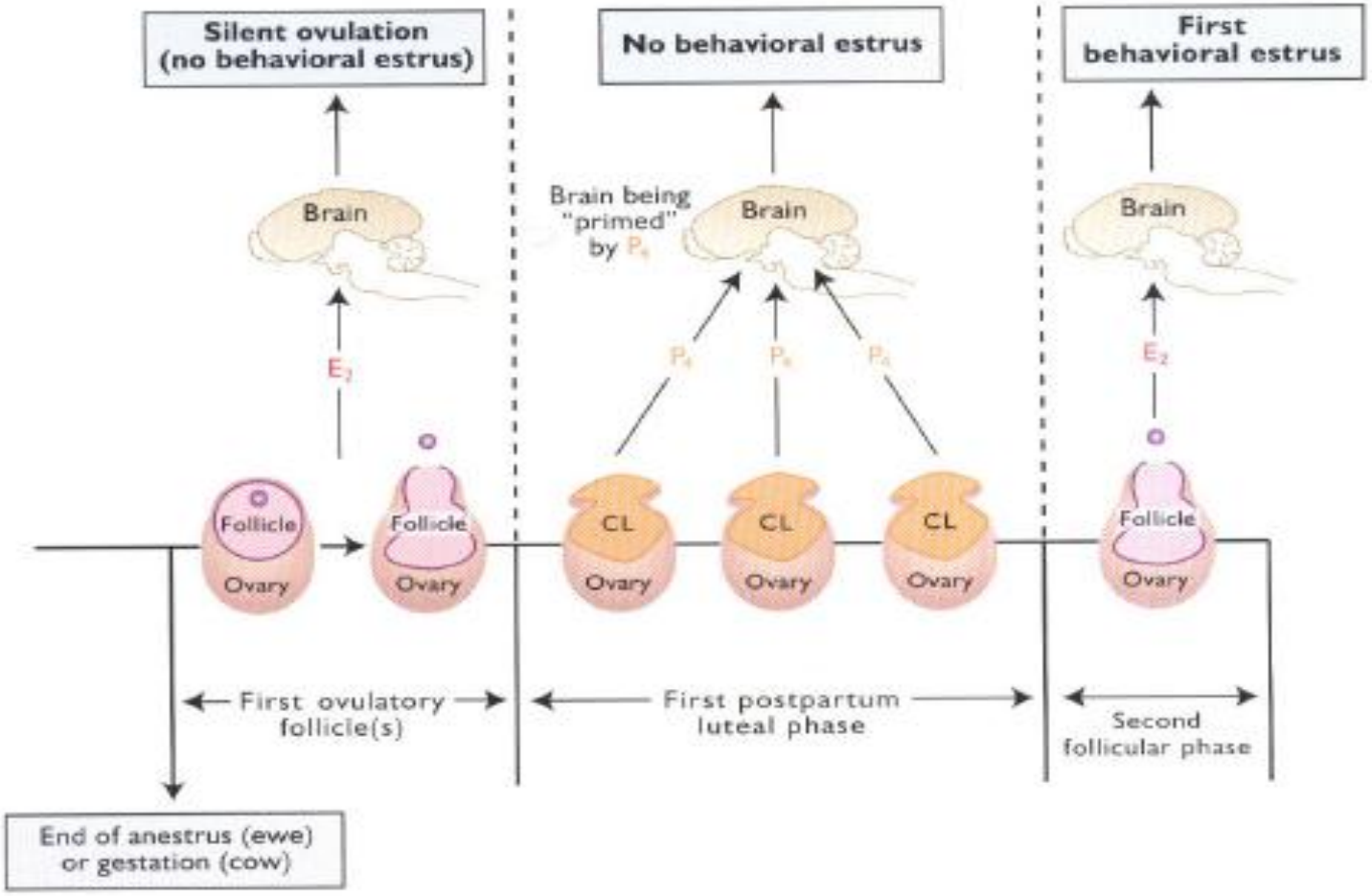


Figure 7-7. The Effect of Photoperiod on Short-Day Breeders

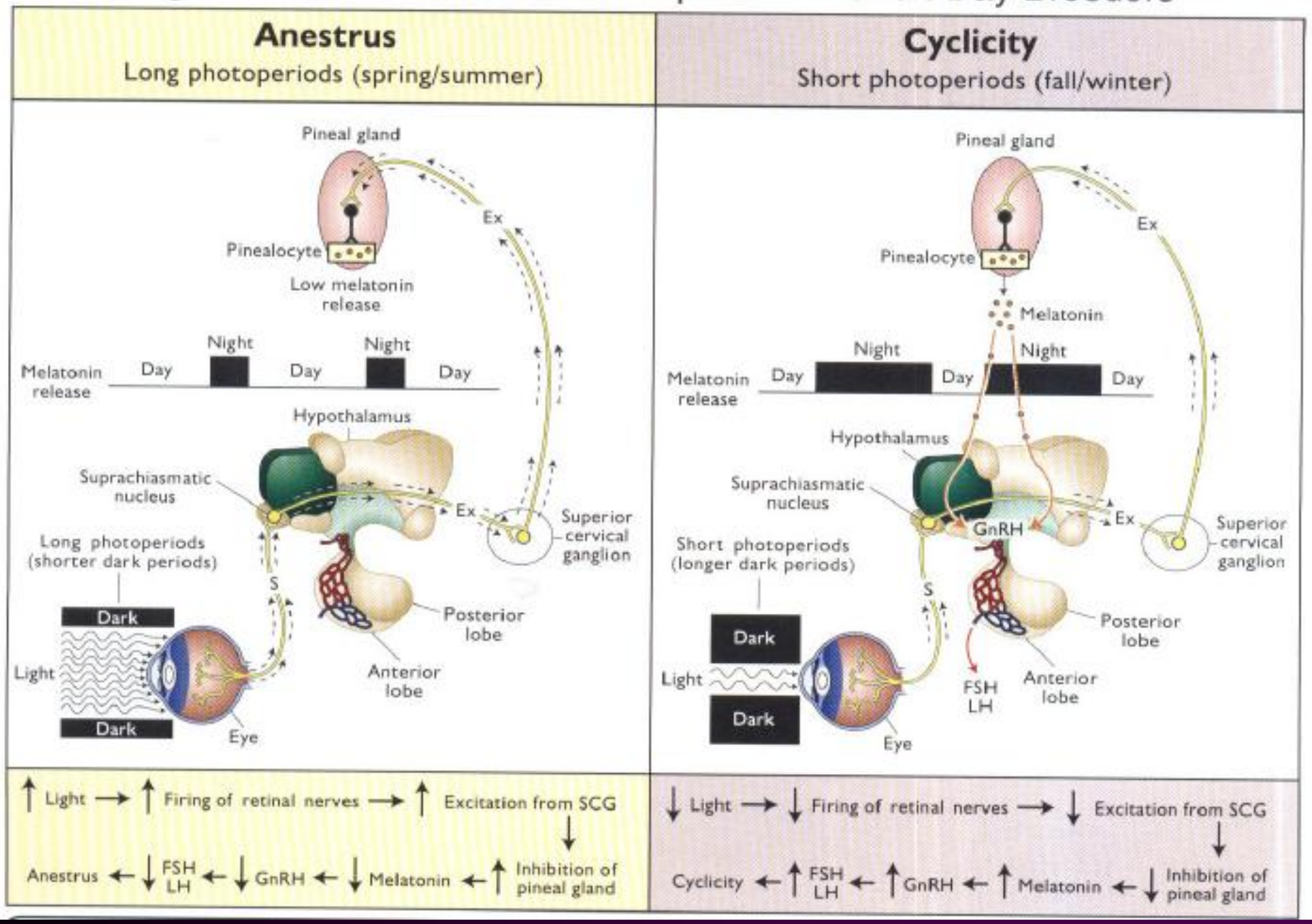


Figure 7-8. Influence of Suckling Frequency Upon Blood LH (a Direct Indication of GnRH Release) in Postpartum Beef Cows

(Derived from the data of Dr. G.L. Williams, Texas A&M University, Beeville)

When the number of suckling sessions is between 3 and 20 per day, amplitude and pulse frequency of blood LH are quite low and the cow remains in anestrus.

When the number of suckling sessions is limited to two or less per day, the amplitude and pulse frequency of LH increases dramatically and the cow will begin to cycle.

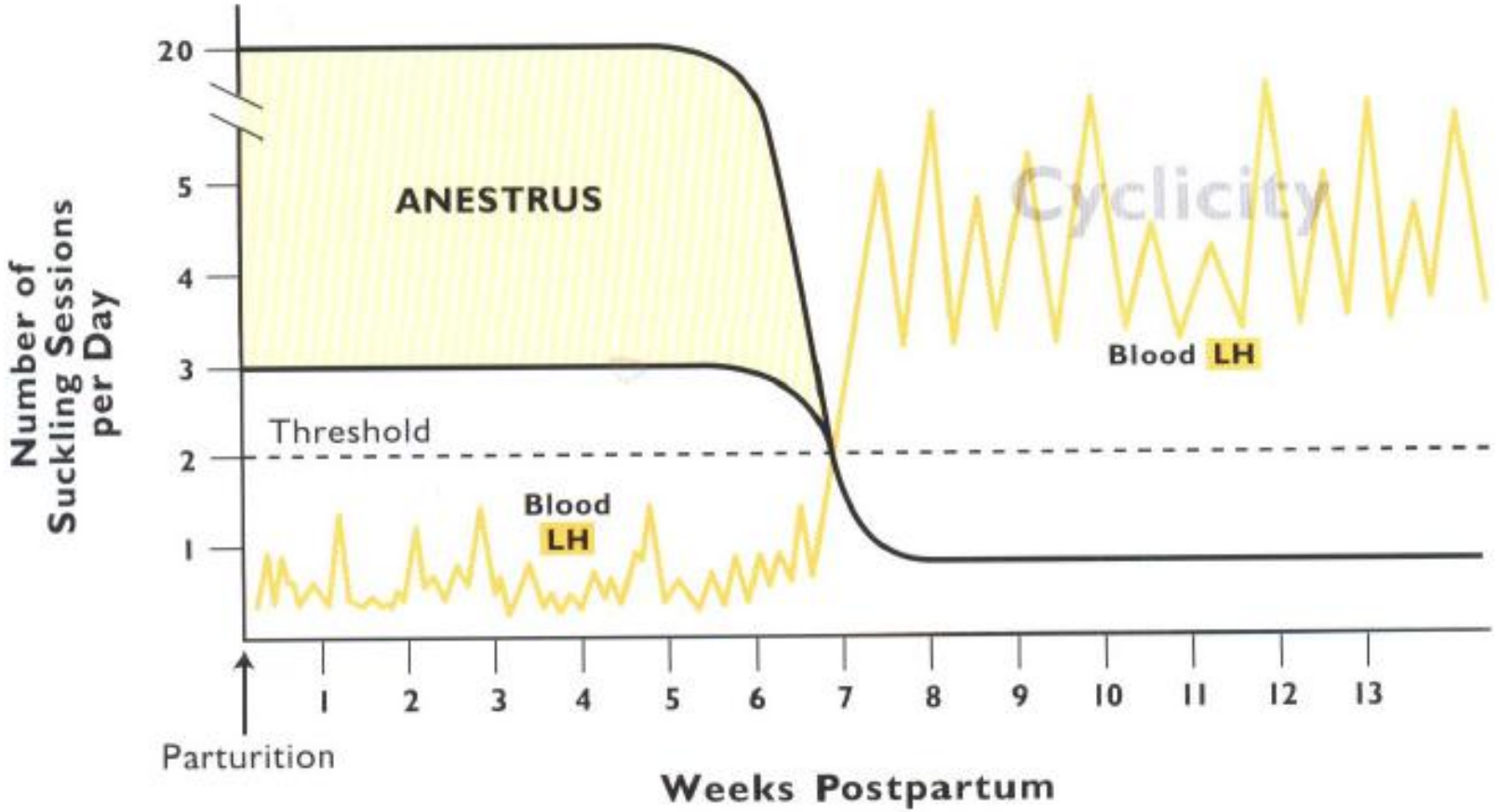
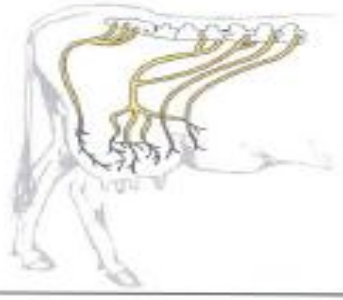
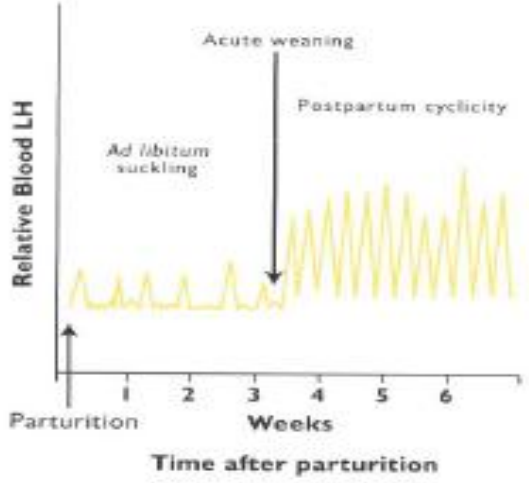


Figure 7-9. *Ad Libitum* Suckling Results in Suppression of LH Amplitude and Pulse Frequency

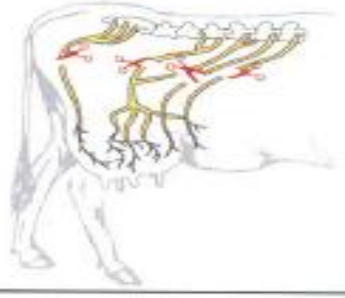
Intact cow



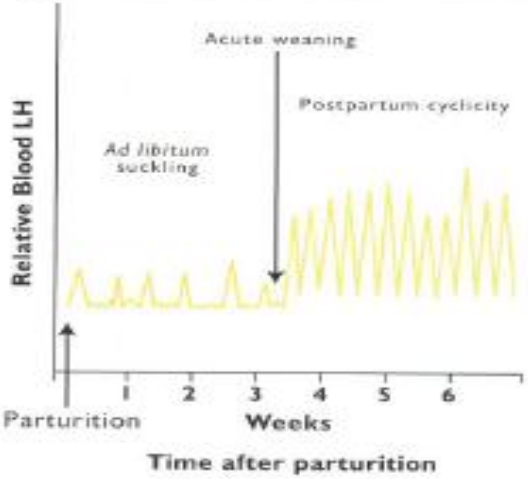
When calves are weaned suddenly from cows with intact mammary nerves, the LH pulse frequency and amplitude increases dramatically.



Mammary denervated cow



In cows with the afferent neural pathway severed, acute weaning causes the same effect as in cows with intact afferent pathways. **Conclusion**--suckling cannot be totally responsible for suppressing LH in the postpartum cow.



Mammary stimulation is not totally responsible for lactational anestrus.

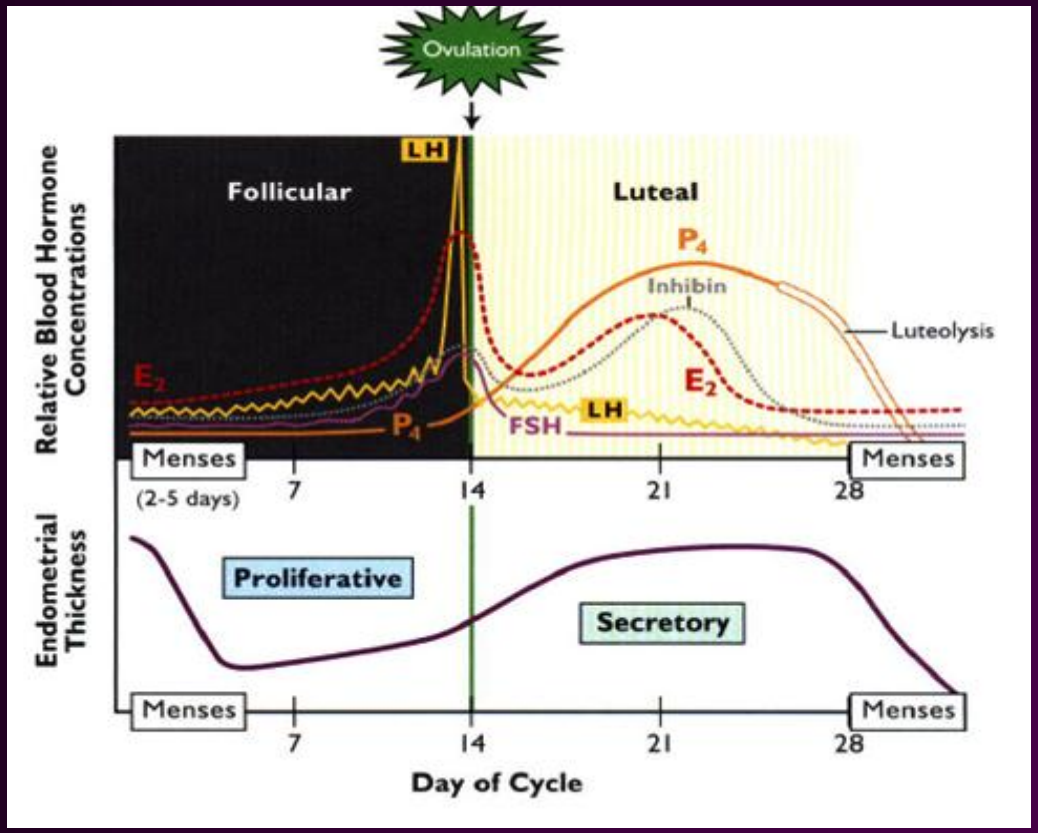
The Menstrual Cycle

The menstrual cycle differs from the estrous cycle in the following ways:

- *there is no defined period of sexual receptivity*
- *there is a period of endometrial sloughing called menses (menstruation)*
- *the timeline for description of the cycle begins and ends with menses, not ovulation or estrus*

Menstrual Cycle

1. Menses Phase (4-6 Days)
2. Proliferative Phase (9 Days)
3. Secretory Phase (14 Days)



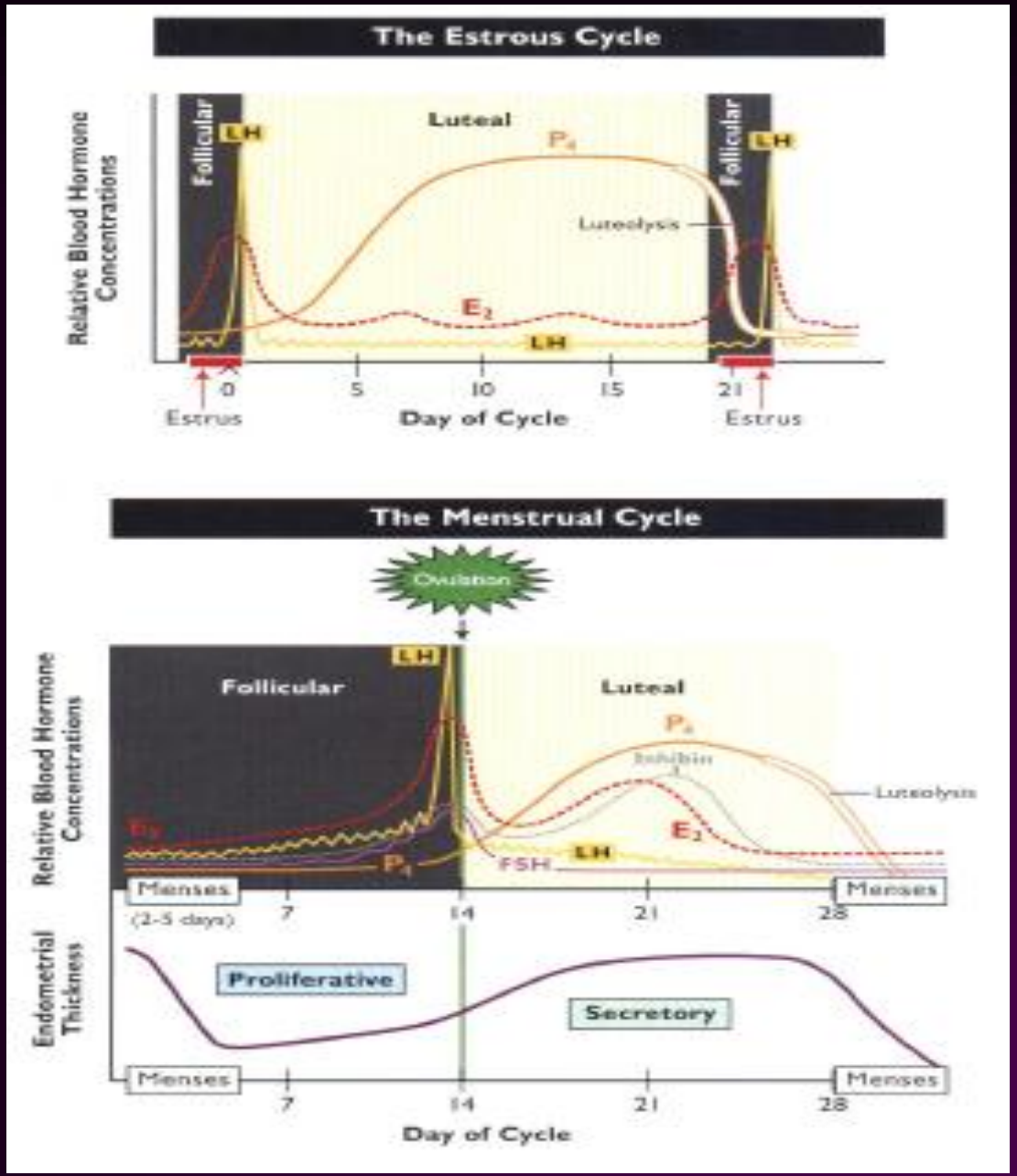

The Estrous Cycle
Relative Blood Hormone Concentrations
Follicular
LH
Luteal
P_4
Luteolysis
E_2
LH
Follicular
LH
0
5
10
15
21
Estrus
Day of Cycle
Estrus
The Menstrual Cycle
Ovulation
Relative Blood Hormone Concentrations
LH
Follicular
Luteal
P_4
Inhibin
Luteolysis
E_2
E_2
P_4
FSH
LH
Menses
(2-5 days)
7
14
21
28
Menses
Endometrial Thickness
Proliferative
Secretory
Menses
7
14
21
28
Menses
Day of Cycle

Table 7-2. Cycle Event Comparison Between the Estrous Cycle and Menstrual Cycle

EVENT	ESTROUS CYCLE	MENSTRUAL CYCLE
Follicular Phase	Short (20% or less of cycle duration)	Long (50% of the cycle duration)
Ovulation	At the beginning and end of the cycle	Middle of cycle (day 14)
Luteal Phase	80% of the cycle	50% of the cycle
Fertile Period	24 hrs or less (5% of cycle)	Up to 6 days before ovulation (18% of cycle)
Endometrial Sloughing	None	After luteolysis
Luteolysis	Uterine $PGF_{2\alpha}$	Ovarian $PGF_{2\alpha}$
Sexual Receptivity	Well defined	Relatively uniform throughout cycle
Progesterone function and sexual receptivity	Inhibits GnRH release Inhibits sexual receptivity	Inhibits GnRH release Does not influence sexual receptivity
Menopause	None described	Well characterized (follicular depletion)

Reproductive Cyclicity - The Follicular Phase

Follicular Phase

Overview:

Follicular phase is initiated after luteolysis that results in a marked reduction in progesterone. Therefore, the negative feedback by progesterone on the hypothalamus is removed and GnRH is realsed at higher amplitudes and frequencies than during the preceding luteal phase. Then LH & FSH…

Significant events during follicular phase

1) Gonadotropin release from the anterior lobe of the pituitary
2) Follicular preparation for ovulation
3) Sexual receptivity
4) ovulation

The tonic and surge centers in the hypothalamus control GnRH release.

Tonic center:

1- Ventromedial Nucleus

2- Arcuate Nucleus

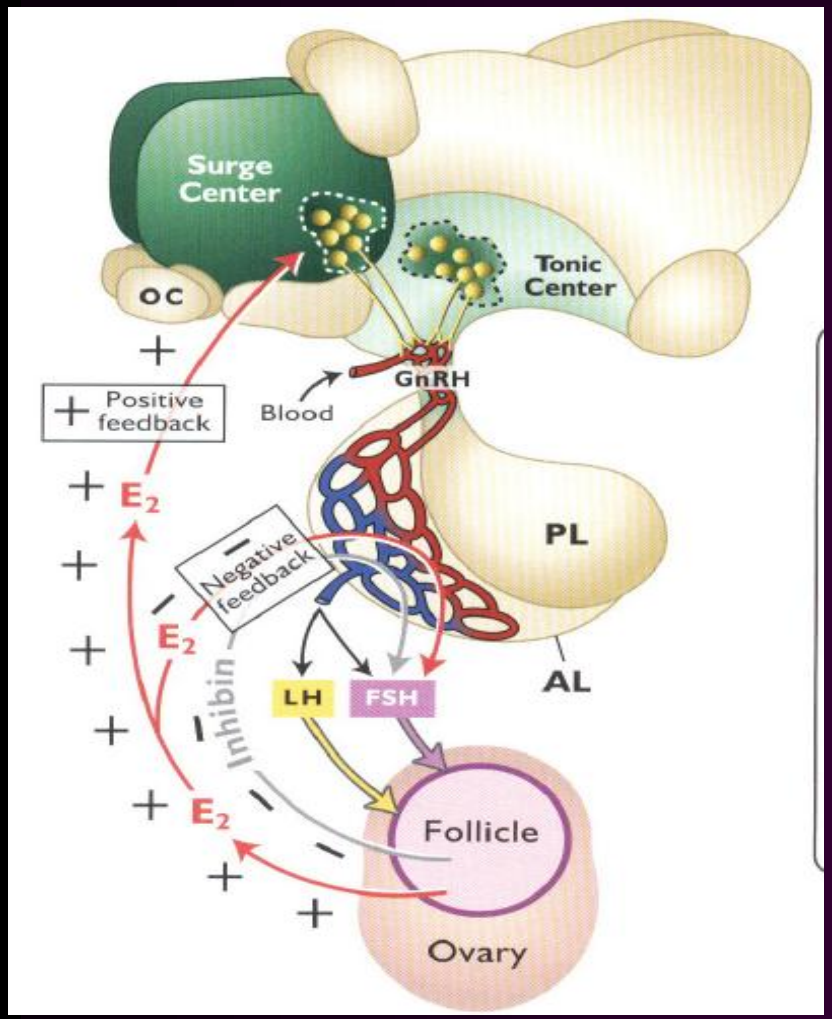
Surge Center:

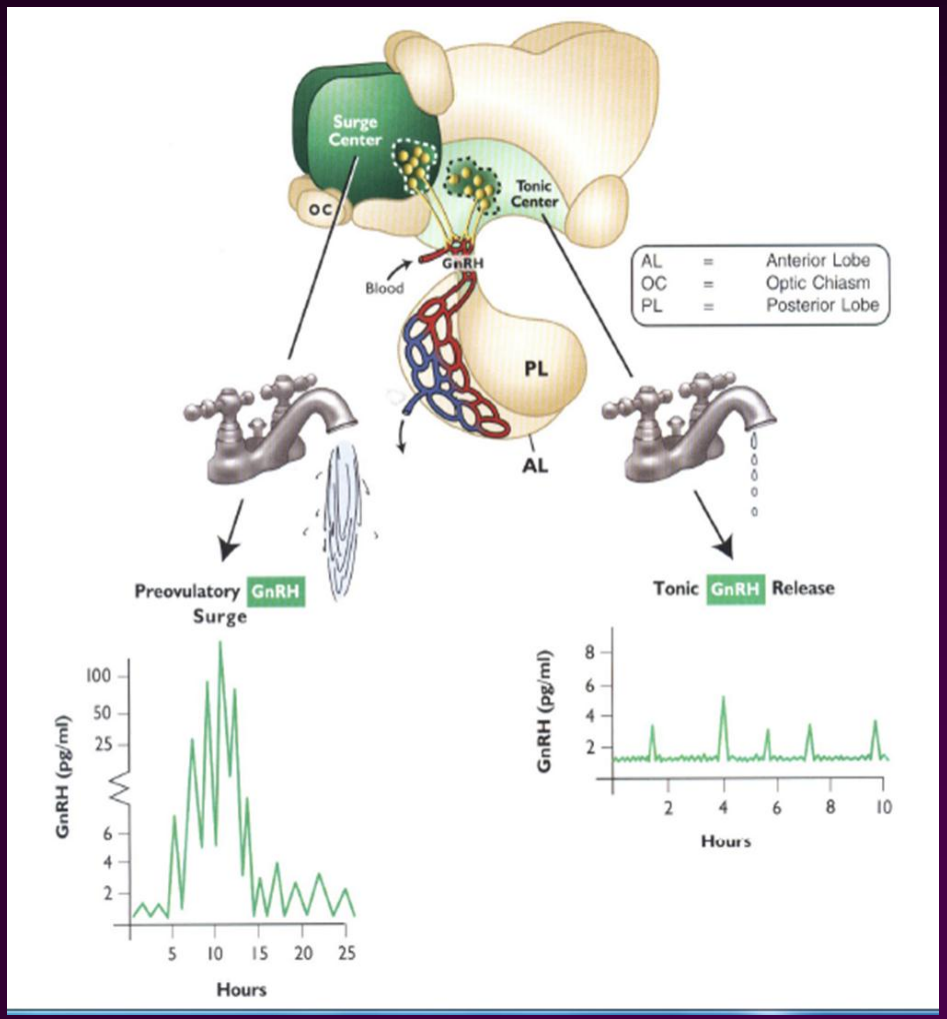
1- Preoptic Nucleus

2- Suprachiasmatic Nucleus

3- Anterior hypothalamic area

- ✓ Tonic center releases basal levels of GnRH until it receives the appropriate positive stimulus. This stimulus is known to be a threshold levels of E2 in the absence of P4.





Note!

GnRH episodes occur every 1.5 to 2 hours during the follicular phase. During the luteal phase episodes of GnRH occur every 4 to 8 hours.

Follicular dynamics

- Follicular dynamics (Growth, Degeneration) occurs continuously throughout the entire estrous cycle.

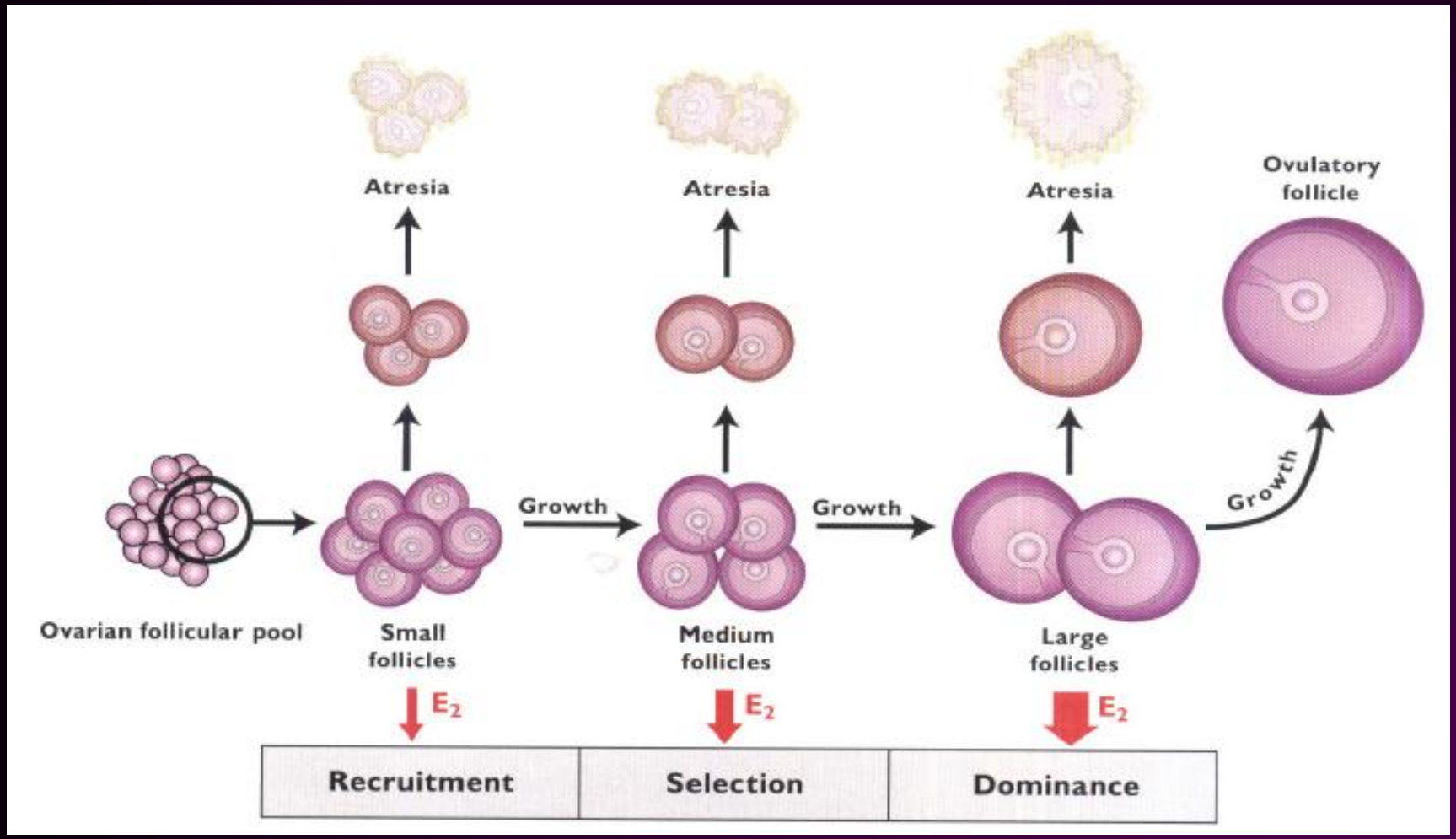
- Antral follicles of various sizes develop in response to tonic levels of FSH and LH and these antral follicles are always present.

Dynamics of antral follicles consist of:

- *recruitment*
- *selection*
- *dominance*
- *atresia*

In Monotocous species (Cow, Mare, Women): single follicle is selected.

In polytocous species (Pig, Dog, Cat): there are multiple dominant follicles.



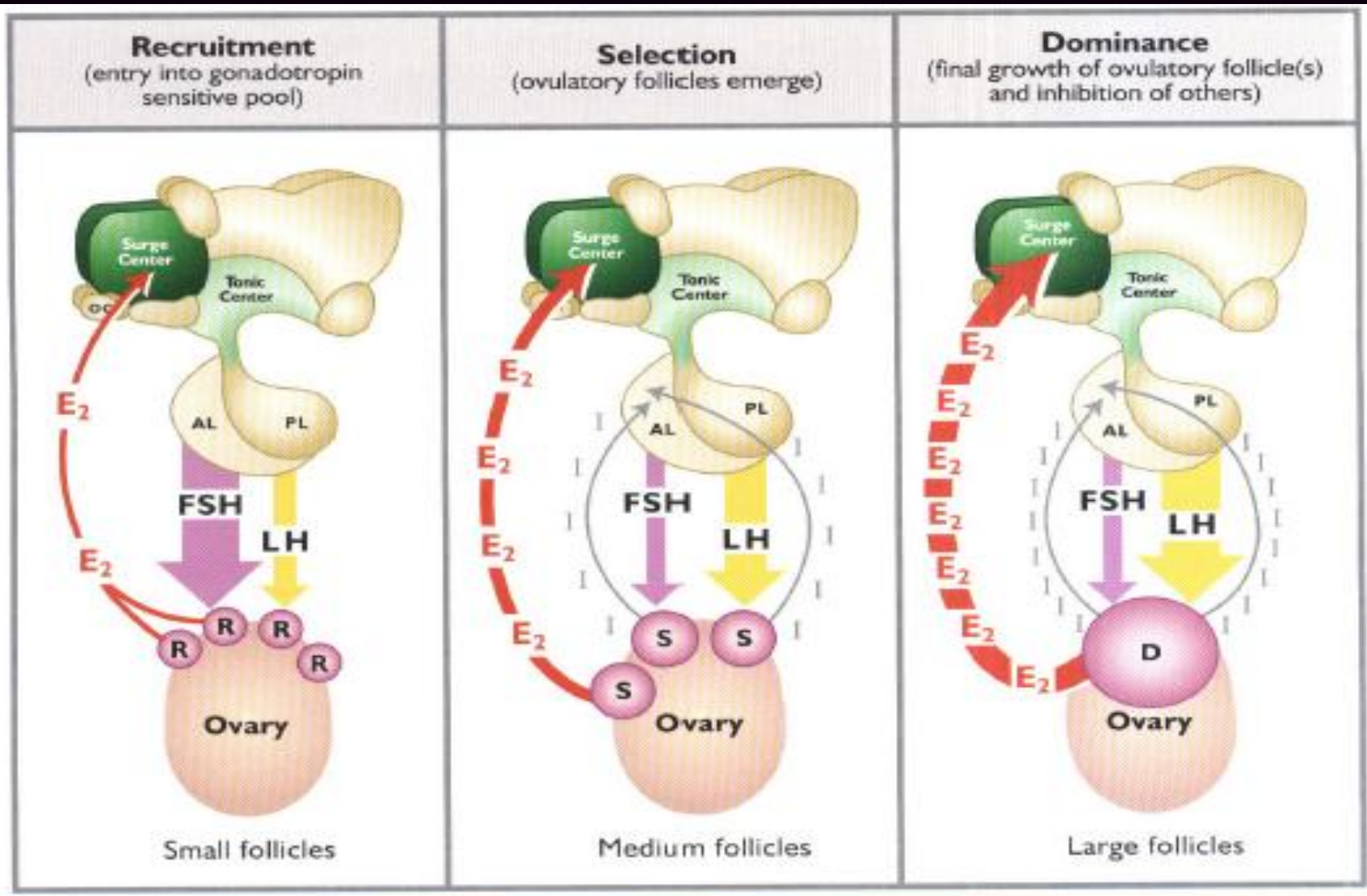
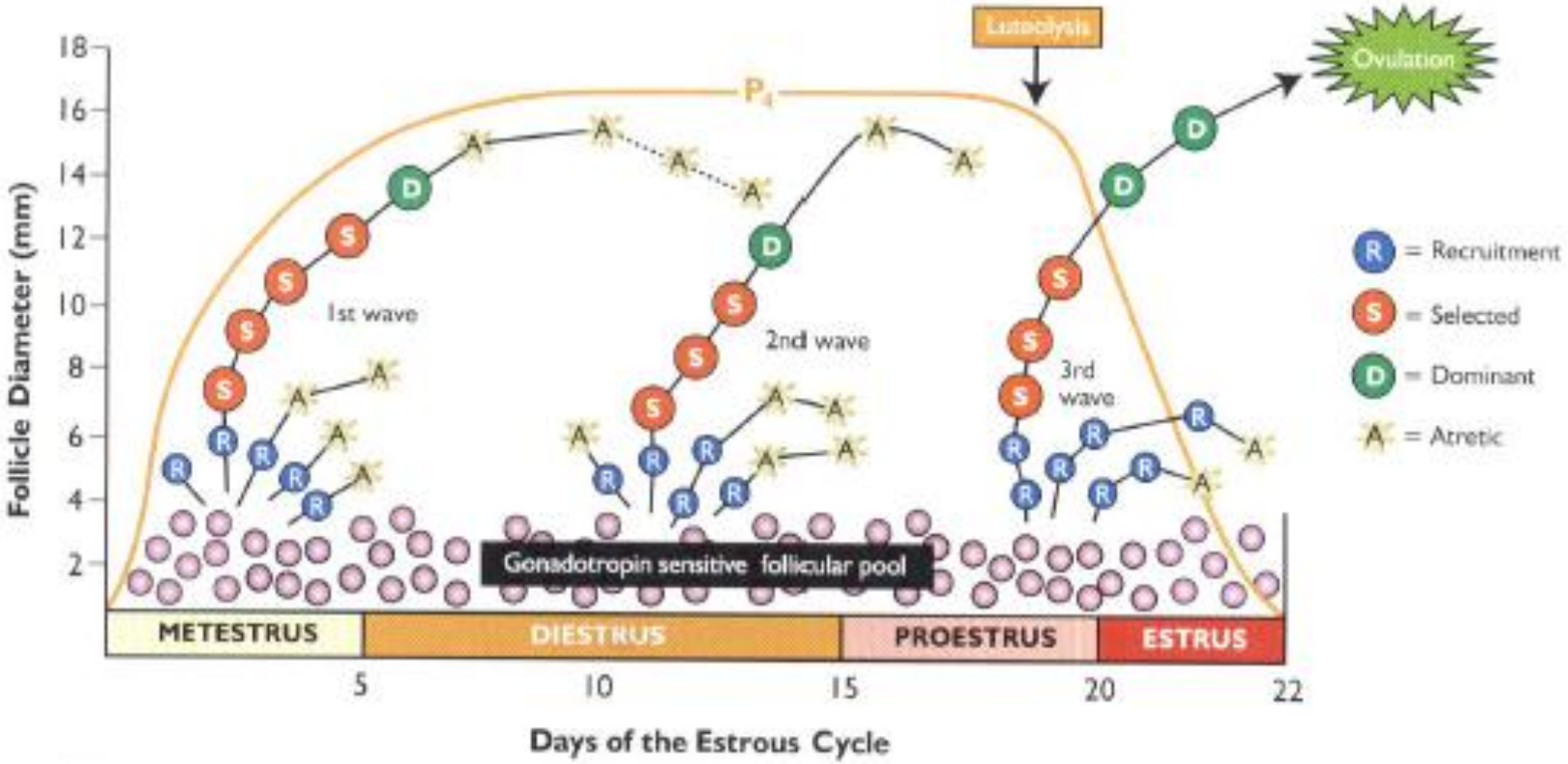

Recruitment
(entry into gonadotropin sensitive pool)
Selection
(ovulatory follicles emerge)
Dominance
(final growth of ovulatory follicle(s) and inhibition of others)
Surge Center
Tonic Center
AL
PL
FSH
LH
E2
R
S
D
Ovary
Small follicles
Medium follicles
Large follicles

Figure 8-7. Several Follicular Waves Occur During One Cycle

(Modified from Lucy et al. 1992)



The first two follicular waves occur either during progesterone elevation (metestrus) or during peak progesterone production (diestrus). Follicles recruited and selected during these phases of the cycle will become atretic.

The last follicular wave (occurring after luteolysis) results in a dominant follicle that will ovulate. Only those follicles recruited during or after luteolysis will become eligible for ovulation. Follicles from any wave that are in the growth phase when luteolysis occurs are capable of ovulation.

Recruitment = high FSH + low LH + no inhibin + no estradiol

Selection = low FSH + moderate LH + low inhibin

Dominance = low FSH + high LH + high inhibin

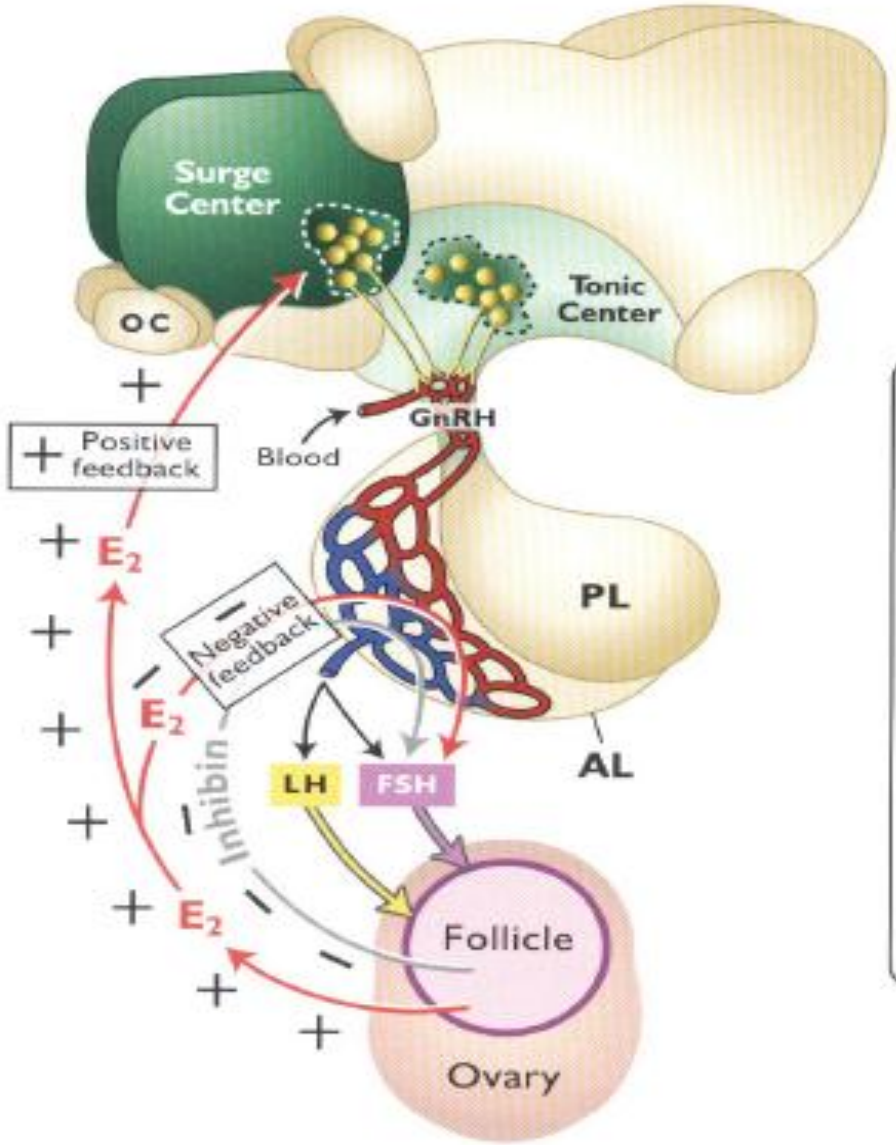
Atresia = degeneration of follicles

Note!

Follicular waves of antral follicles are not unique to the estrous or menstrual cycle.

They occur during before puberty, pregnancy, during anestrus and puerperium (however during these times do not yield dominant follicles that produce threshold levels of estradiol).

Figure 8-2. The Relationship Between the Hypothalamus, the Pituitary and the Ovary During the Follicular Phase



AL	=	Anterior Lobe
E_2	=	Estradiol
OC	=	Optic Chiasm
PL	=	Posterior Lobe

Early in the follicular phase, GnRH pulse frequency begins to increase (because of low P_4), thus causing FSH and LH to be secreted from the anterior lobe of the pituitary. These gonadotropins stimulate ovarian follicles to secrete estradiol, a positive feedback on the neurons of the hypothalamic surge center occurs and the GnRH neurons secrete a burst of GnRH (See Figure 8-3). Later in the follicular phase, the follicle secretes inhibin that causes a negative feedback on FSH secretion from the anterior lobe of the pituitary. Our present understanding is that E_2 also is involved in suppression of FSH at the anterior lobe level.

"The 2-Cell, 2-Gonadotropin Model"
Describe Estrogen Synthesis

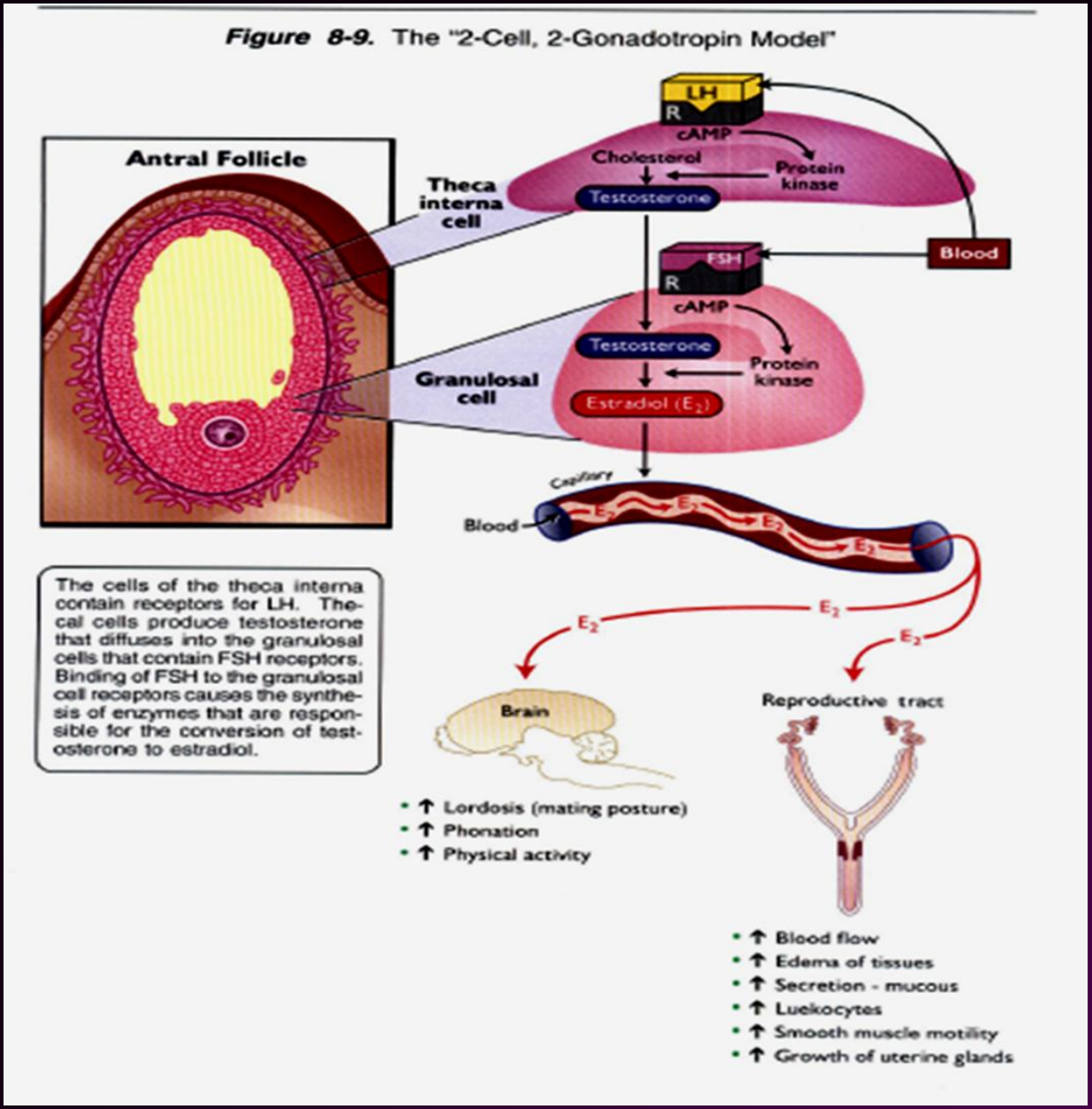
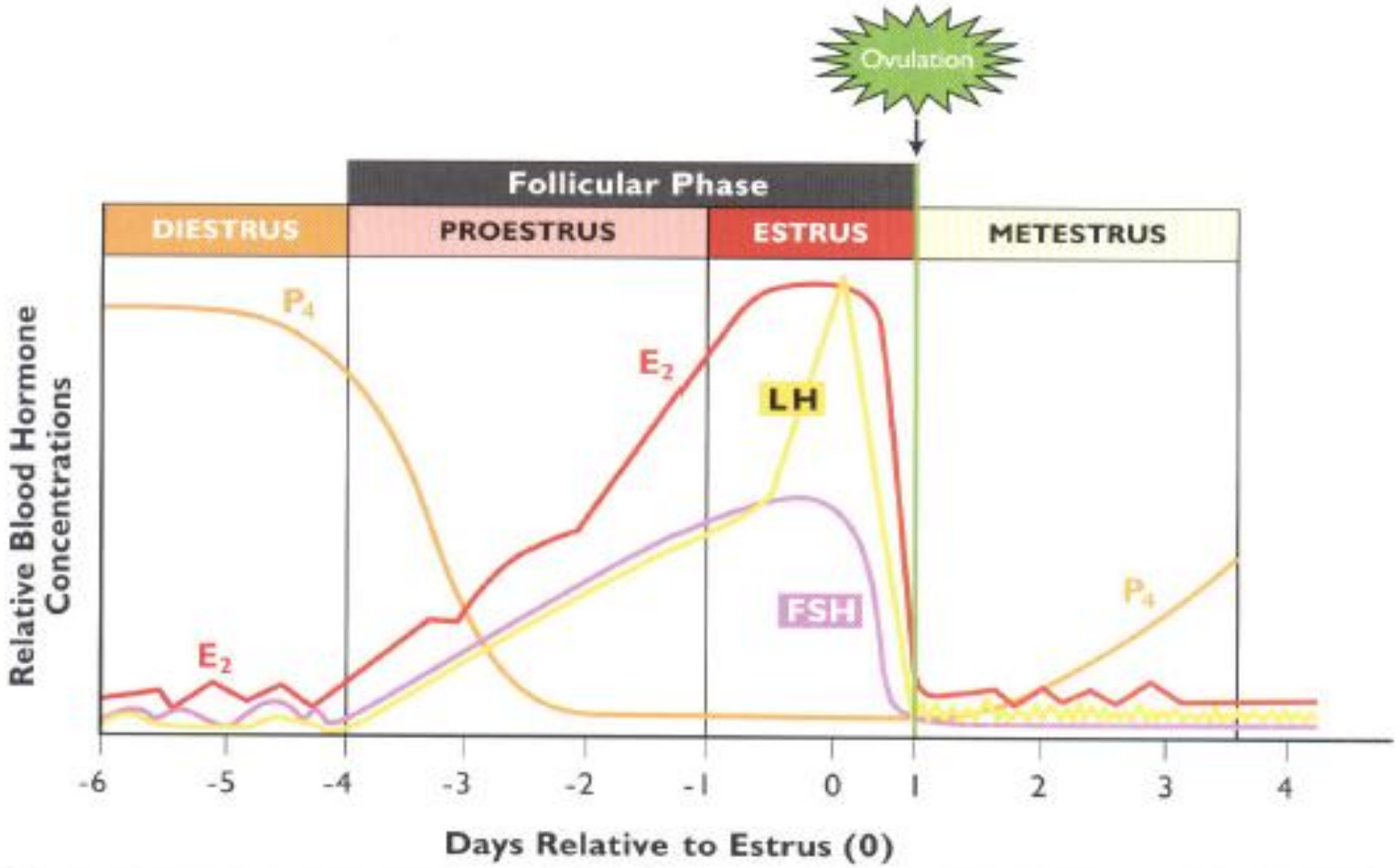


Figure 8-4. Hormonal Changes During the Follicular Phase



Proestrus

As progesterone (P_4) drops, FSH and LH increase together in response to GnRH. FSH and LH cause the production of estradiol (E_2) by ovarian follicles (See Figure 8-2).

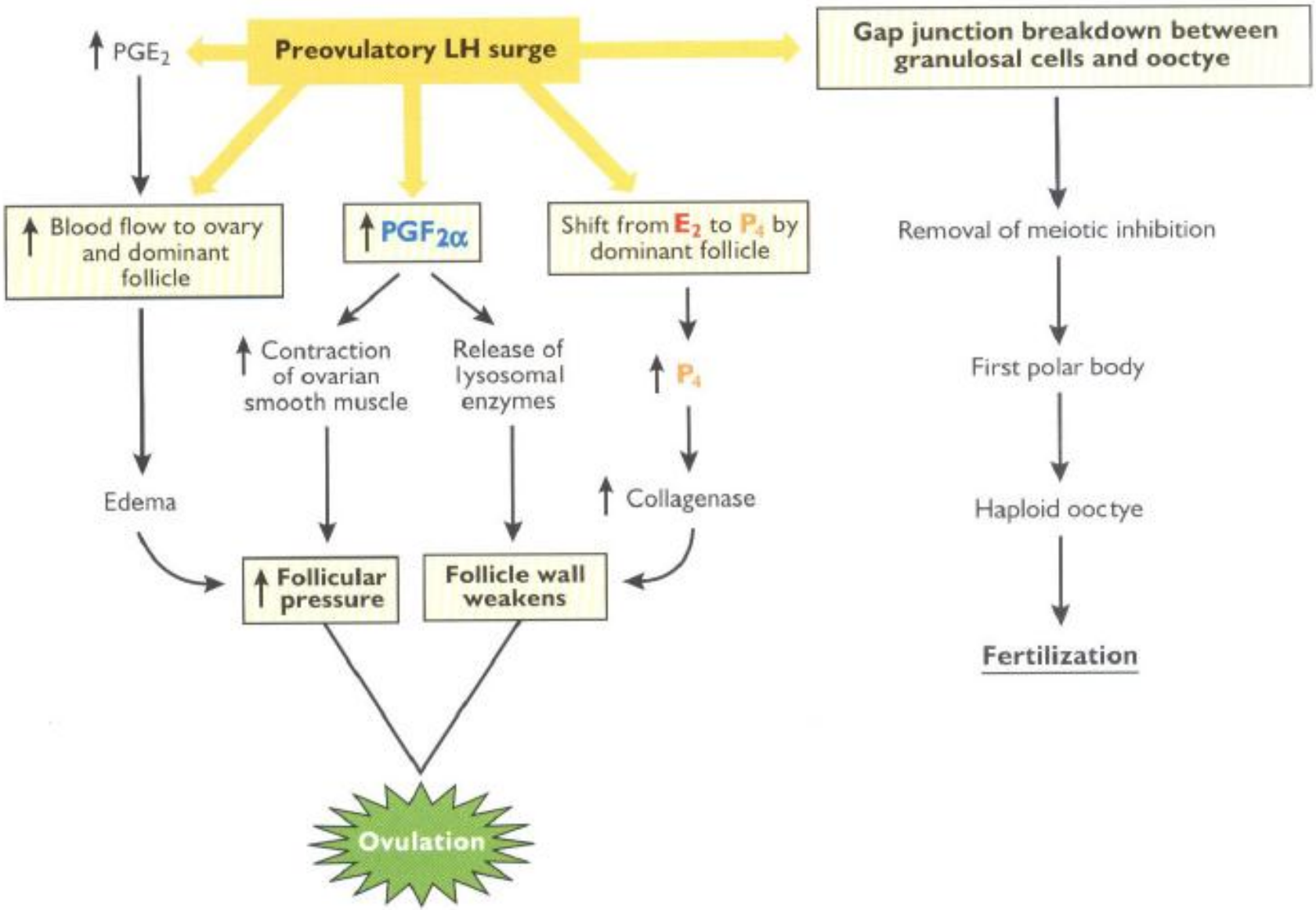
Estrus

When recruited follicles develop dominance, they produce estradiol and inhibin that suppresses FSH secretion from the anterior lobe of the pituitary. Thus, FSH does not surge with the same magnitude as LH. When estrogen reaches a threshold level (peak), the preovulatory surge of LH occurs, inducing ovulation.

The major effects of estrogen on the reproductive tract are:

- ***increased blood flow***
- ***genital swelling***
- ***change in tissue electrical conductivity***
- ***leukocytosis***
- ***increased mucosal secretion***
- ***initiation of uterine gland growth***
- ***elevated myometrial tone***

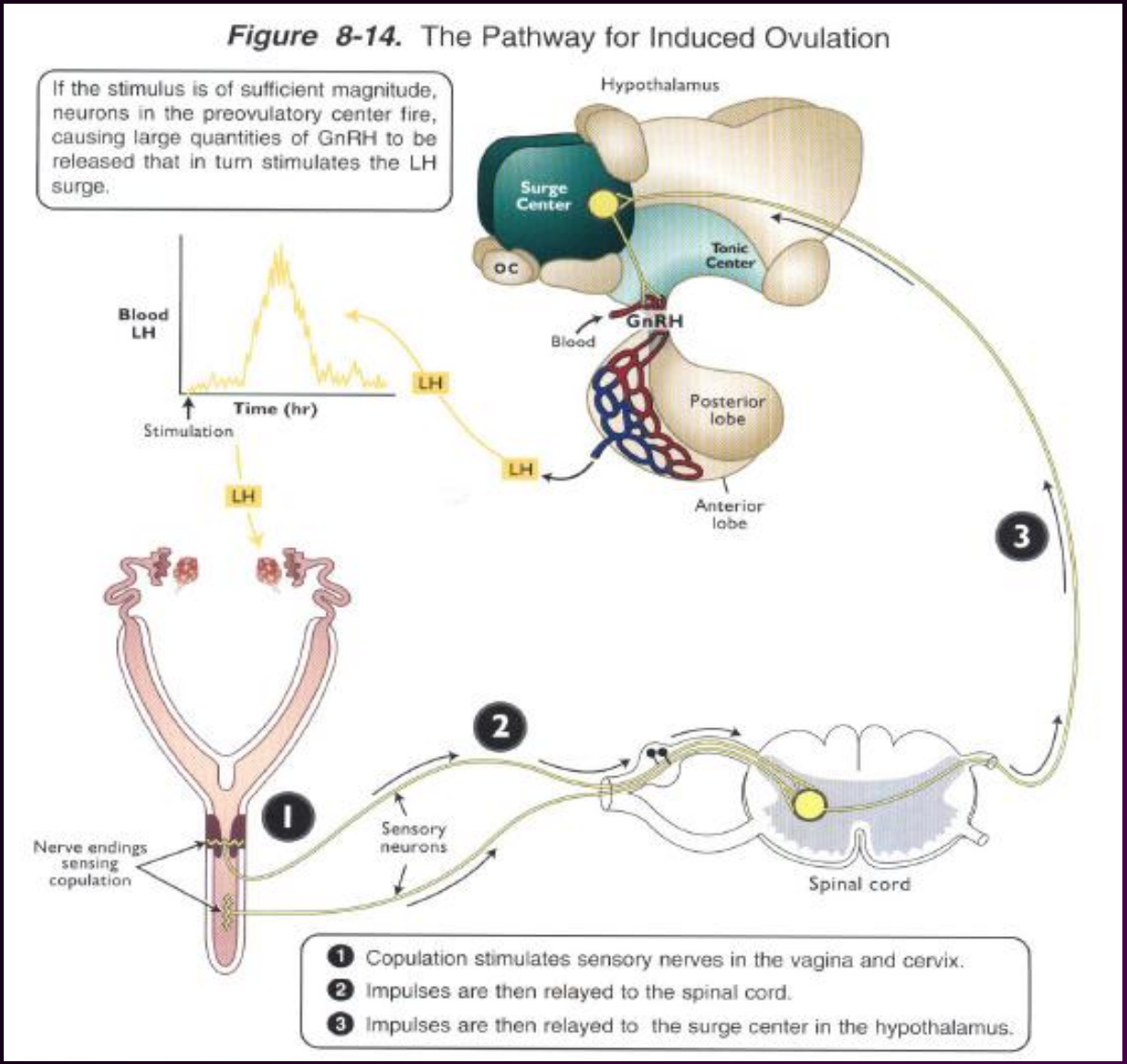
Figure 8-13. Ovarian Events Caused by the Preovulatory LH Surge



Ovulation is brought about by:

- *elevated blood flow*
- *breakdown of connective tissue*
- *ovarian contractions*

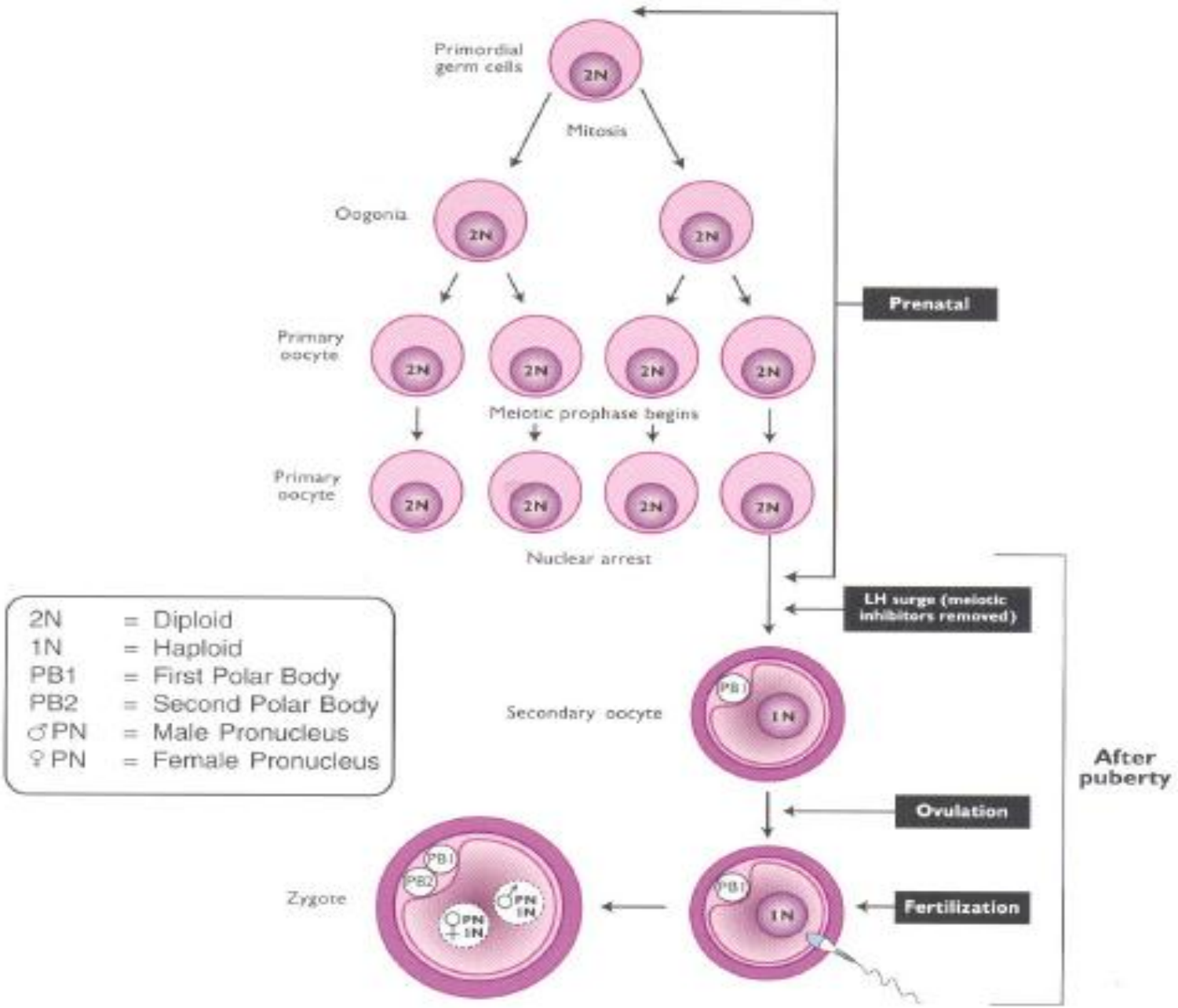
Some species require copulation before ovulation can occur



The four phases of oocyte maturation are:

- *mitotic division of primordial germ cells (prenatal)*
- *nuclear arrest (dictyotene)*
- *cytoplasmic growth*
- *resumption of meiosis*

Figure 8-16. The Major Steps of Oogenesis



Thanks for your attention