Reproductive Physiology in Domestic Animals

Part two

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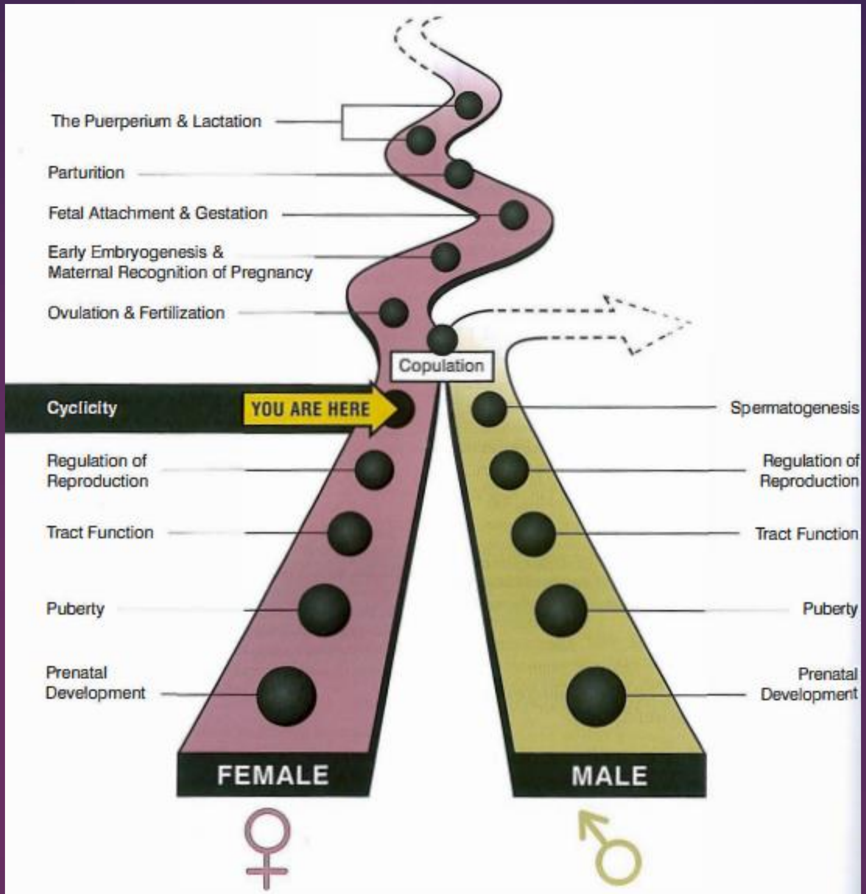

Section VI

Reproductive cyclicity

Terminology and Basic Concepts

The Estrous Cycle

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- 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 reproductive events beginning at estrus (heat) and ending at the subsequent estrus.
- They can be interrupted by pregnancy, nursing, season of the year in some species, inadequate nutrition, stressful environmental conditions, anestrous, and pathologic conditions of the reproductive tract.
- The word “Estrous” or “Oestous” refers to the cycle and its an adjective but “estrus” is a noun and refers to the behavior.

Types of Estrous Cycles

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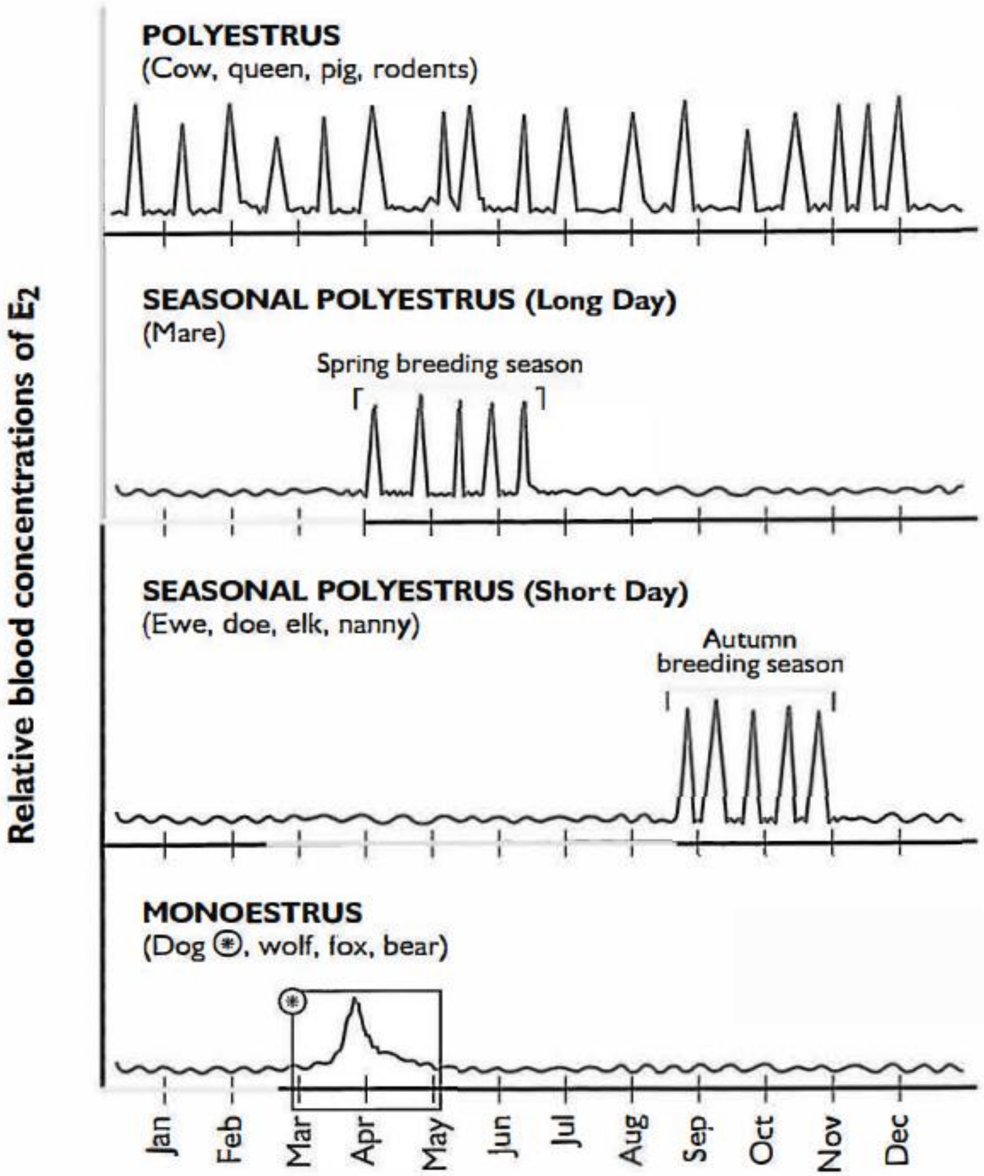
- Estrous cycles are categorized according to the frequency of occurrence throughout the year. These classifications are polyestrus, seasonally polyestrus and monoestrus



Phases of the Estrous Cycle

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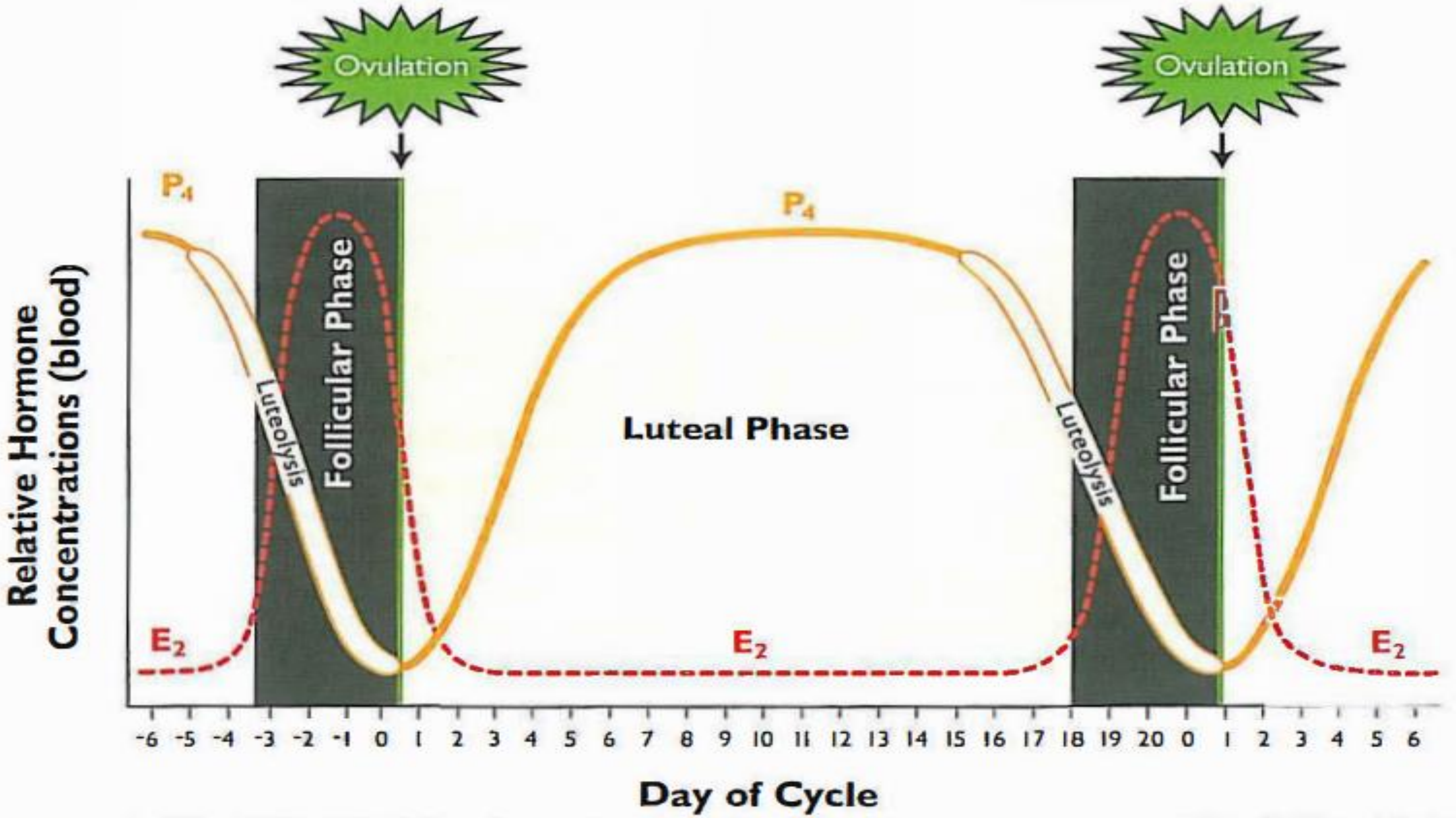
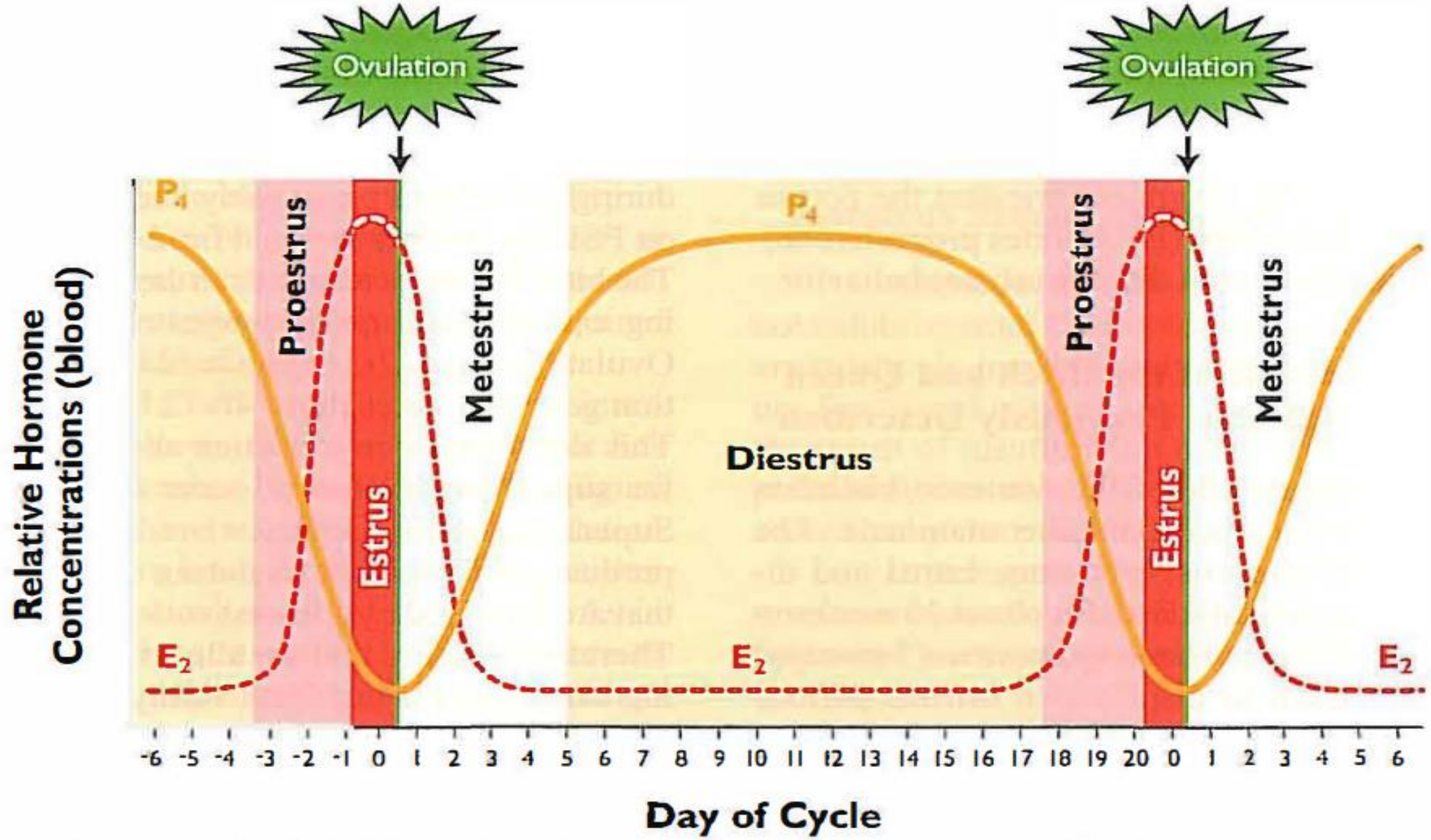


The follicular phase begins after luteolysis that causes the decline in progesterone. Gonadotropins (FSH and LH) are therefore secreted that cause follicles to secrete estradiol (E_2). The follicular phase is dominated by estradiol secreted by ovarian follicles. The follicular phase ends at ovulation. Estrus is designated as day 0.

The luteal phase begins after ovulation and includes the development of corpora lutea that secrete progesterone (P_4). The luteal phase also includes luteolysis that is accompanied by a rapid drop in progesterone. Luteolysis is brought about by prostaglandin $F_{2\alpha}$.

Stages of the Estrous Cycle



Proestrus is characterized by a significant rise in estradiol (E_2) secreted by maturing follicles.

When estradiol reaches a certain level, the female shows behavioral estrus and then ovulates.

Following ovulation, cells of the follicle are transformed into luteal cells that form the corpus luteum (CL) during metestrus.

Diestrus is characterized by a fully functional CL and high progesterone (P_4).

The Estrous Cycle of the Bitch

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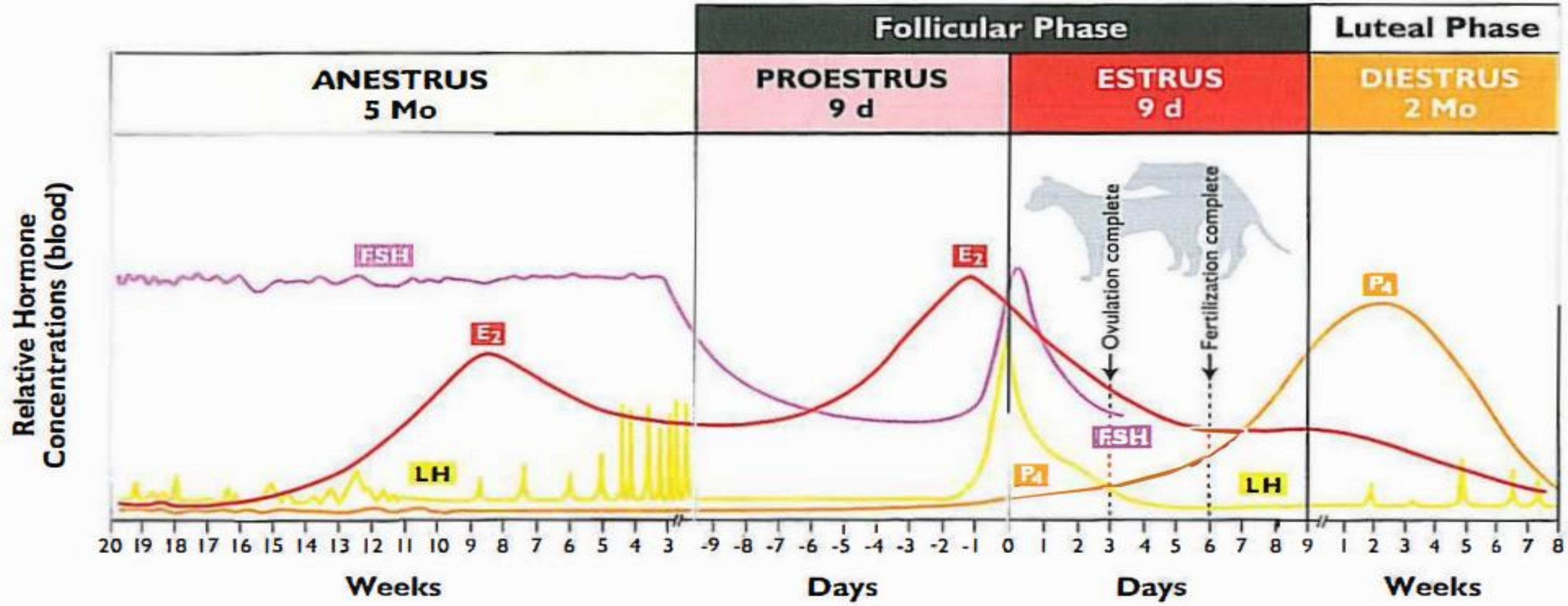

Anestrus
A period of reproductive quiescence. This long anestrus period is responsible for a cyclic profile of three cycles in two years.

Proestrus
Proestrus is considered the beginning of the cycle and is characterized by the appearance of a blood-tinged vaginal discharge. It ends when the bitch copulates with the male. 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.

The Estrous Cycle of the Queen

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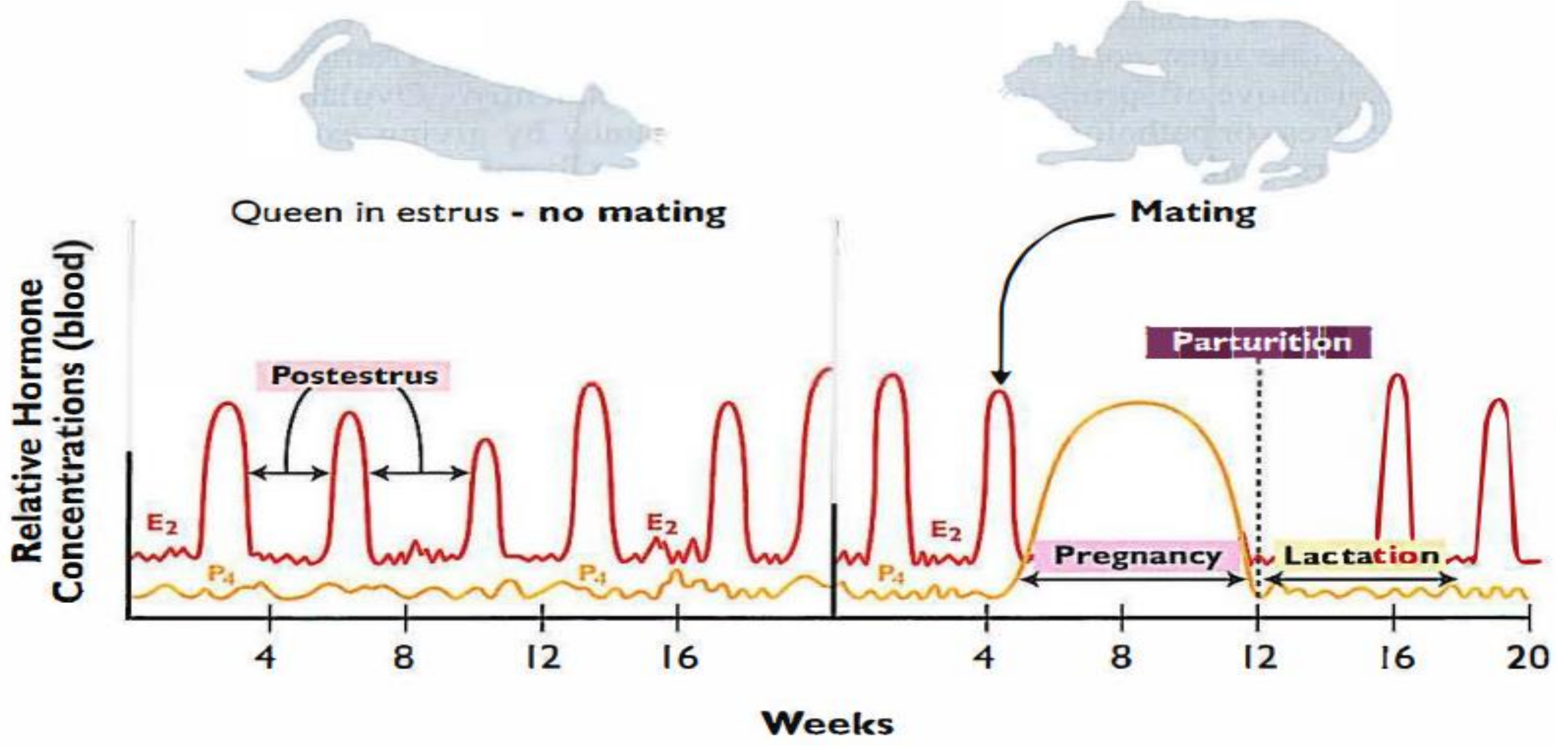

A queen enters estrus (about 9 days) every 17 days. If copulation does not occur, the queen enters a postestrus phase and comes into estrus a few days later. Since the queen is an induced ovulator, when mating does not occur, ovulation does not occur and a CL is not formed.

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 lactating.

Estrous Cycles in Domestic Animals

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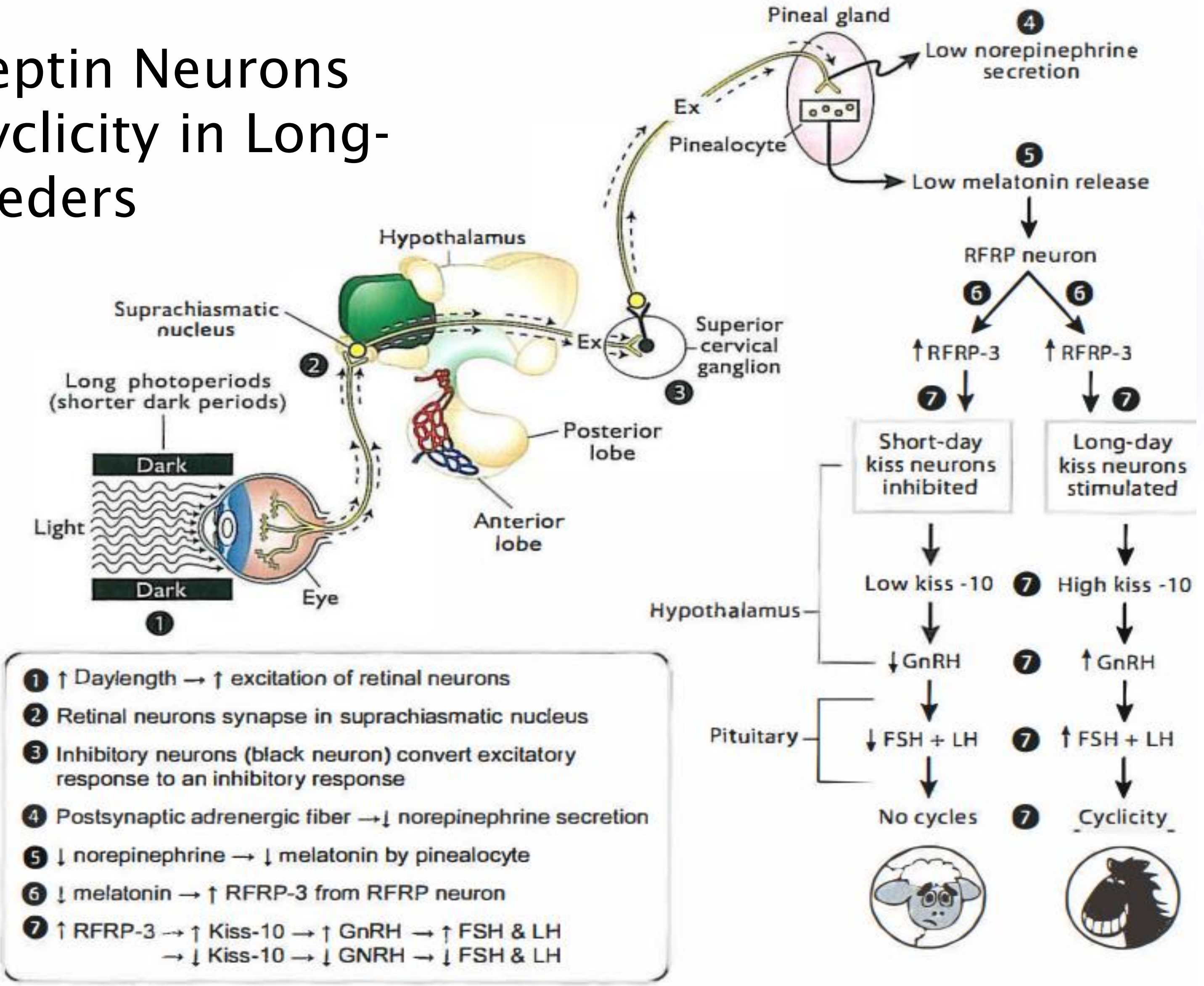
Species	Classification	Length of Estrous Cycle: Mean	Length of Estrous Cycle: Range	Duration of Estrus: Mean	Duration of Estrus: Range	Time From Onset of Estrus to Ovulation	Time From LH Surge to Ovulation
Alpaca	Polyestrus	15d	(11-18d)	5d	(4-5d)	Induced Ovulator	26-36h
Bitch	Monoestrus	6 mo	(3-9 mo)	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

Long-day vs. Short-day Breeders

- Possible Role of Kisspeptin Neurons in the Regulation of Cyclicity in Long-Day and Short-Day Breeders



- RFRP: arg-phe related protein

Lactational Anestrus

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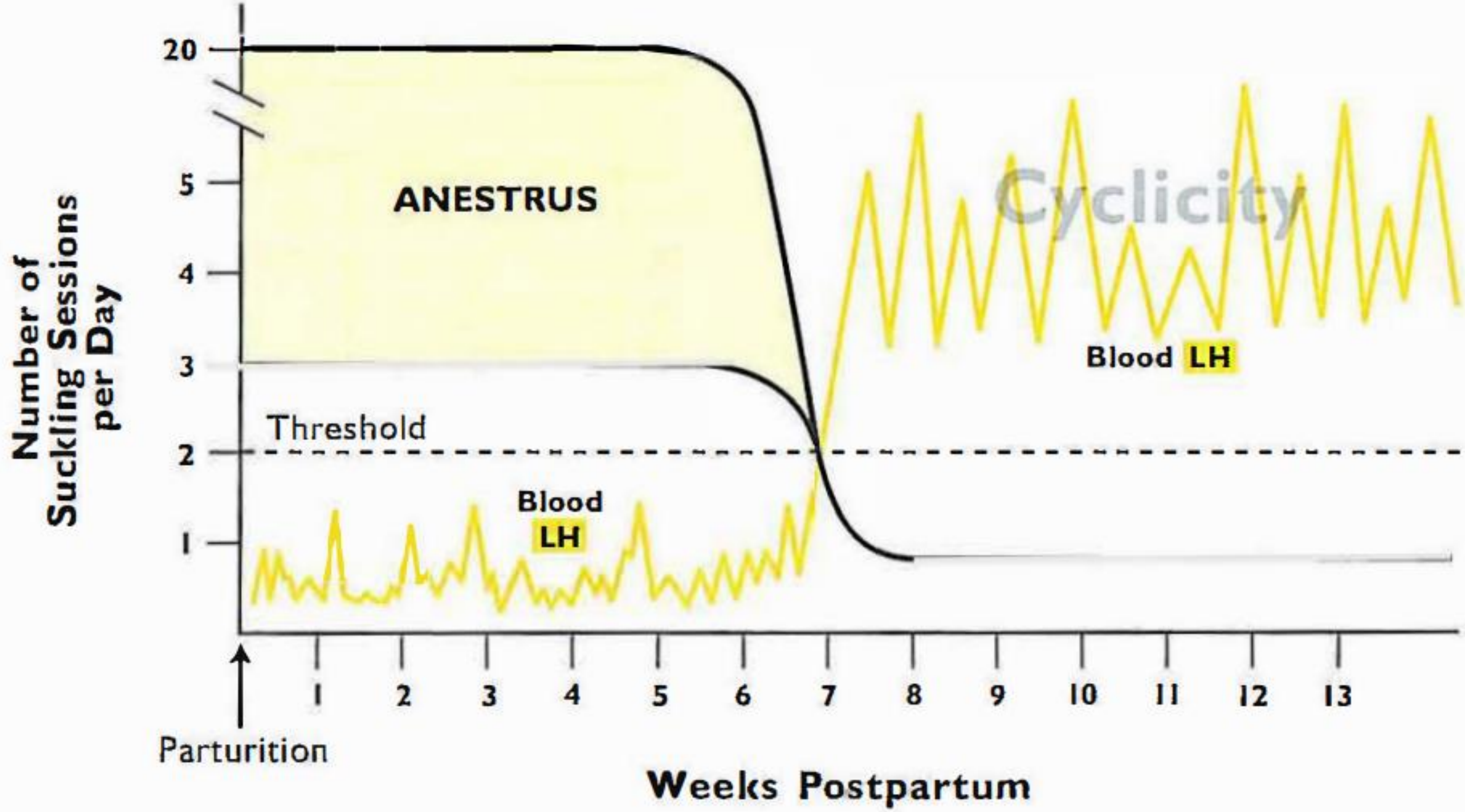
When the number of suckling sessions is between 3 and 20 per day, amplitude and pulse frequency of blood LH are quite low and the cow remains in anestrus.

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.



Lactational Anestrus

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- Almost all mammalian females nursing their young experience lactational anestrus that lasts for variable periods of time.
  - The mare and the alpaca do not experience lactational anestrus.
  - The sow will display estrus and ovulate within 4 to 8 days after weaning.
  - The duration of lactational anestrus is influenced by the degree of suckling in the cow
    - Direct neural stimulation of the mammary gland does not inhibit gonadotropin release in the cow.
    - Visual, olfactory and auditory encounter with the offspring would inhibit GnRH.
  - The bitch does not have lactational anestrus because the anestrus that occurs normally during the cycle lasts about 4-5 months in the presence or absence of lactation.
  - Many queens display estrus and ovulate seven to ten days after parturition. Some of these queens will be bred and conceive during the time that they are lactating.

Lactational Anestrus

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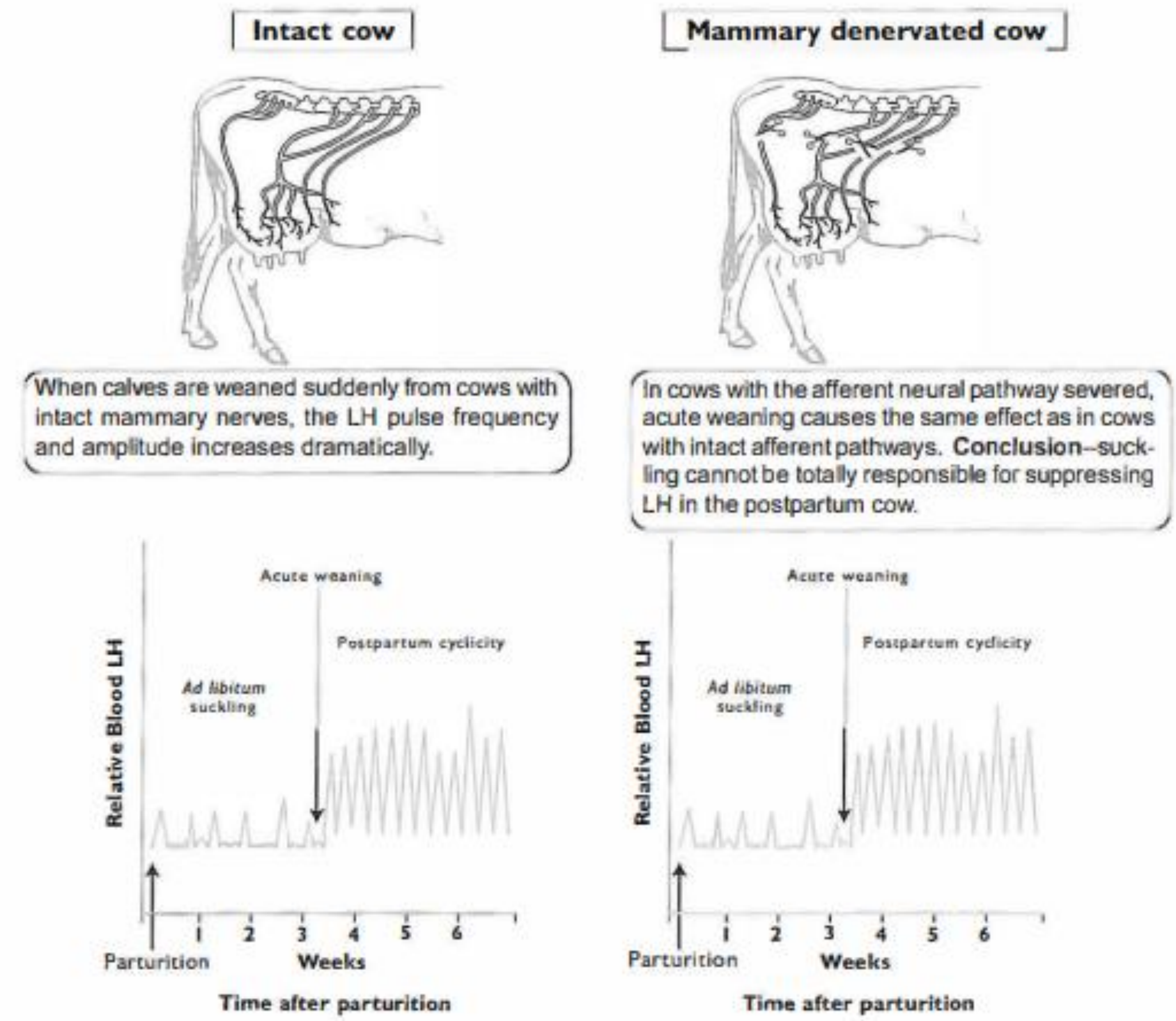

The Estrous Cycle vs. the Menstrual Cycle

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- The **estrous cycle** begins, and ends, with estrus and/or ovulation. The follicular phase is short and the luteal phase long.
- The **menstrual cycle** begins (day 0) and ends with the start of menses (day 28). Ovulation occurs in the middle of the cycle. The follicular and the luteal phase are about the same length (about 14 days each).
    - During the initial 3-5 days of the proliferative phase the endometrium decreases rapidly in thickness because it is sloughed to the exterior during menses. With rising E2, the endometrium begins to proliferate and increase in thickness. After ovulation, the CL produces P4 that causes further proliferation and initiates secretory activity of the endometrium. Luteolysis initiates another menstrual period.

The Estrous Cycle vs. the Menstrual Cycle

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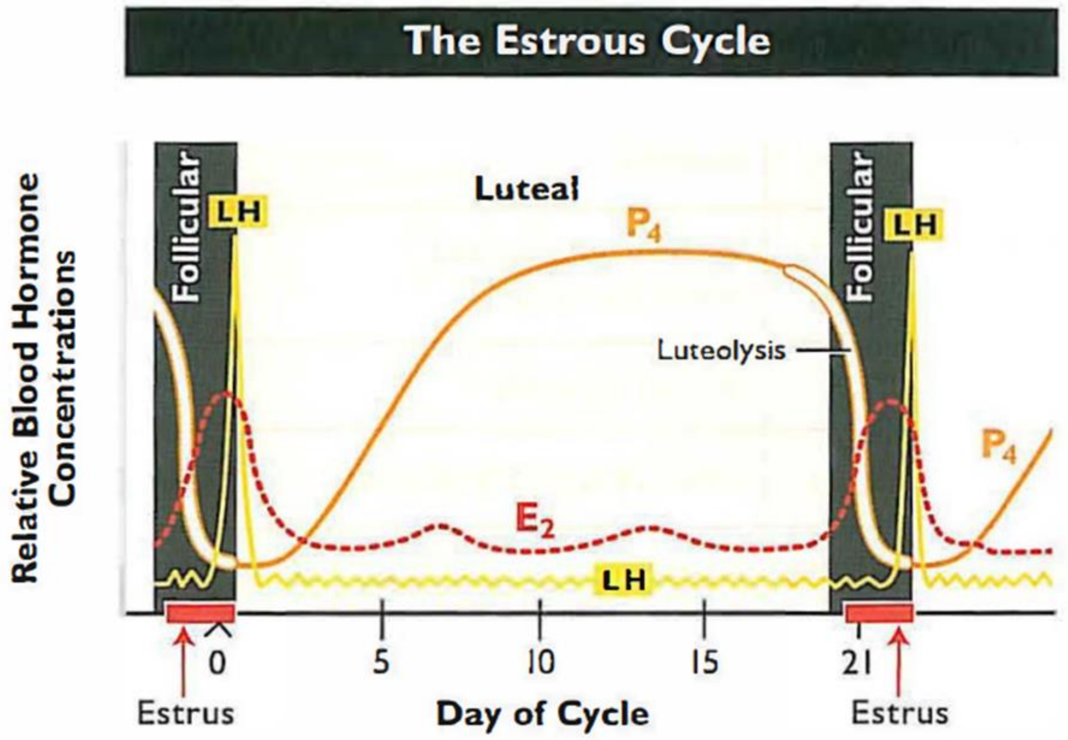

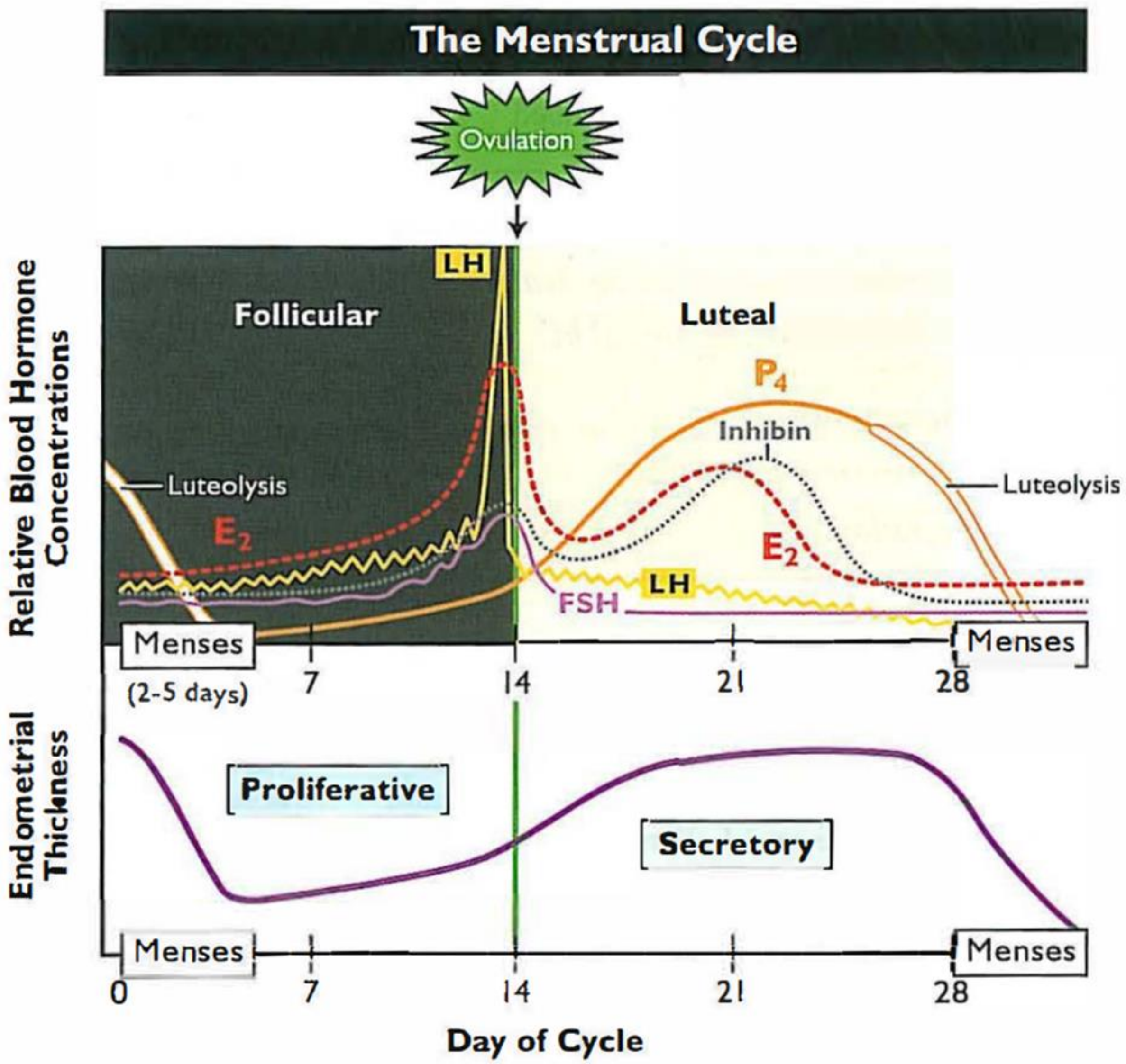

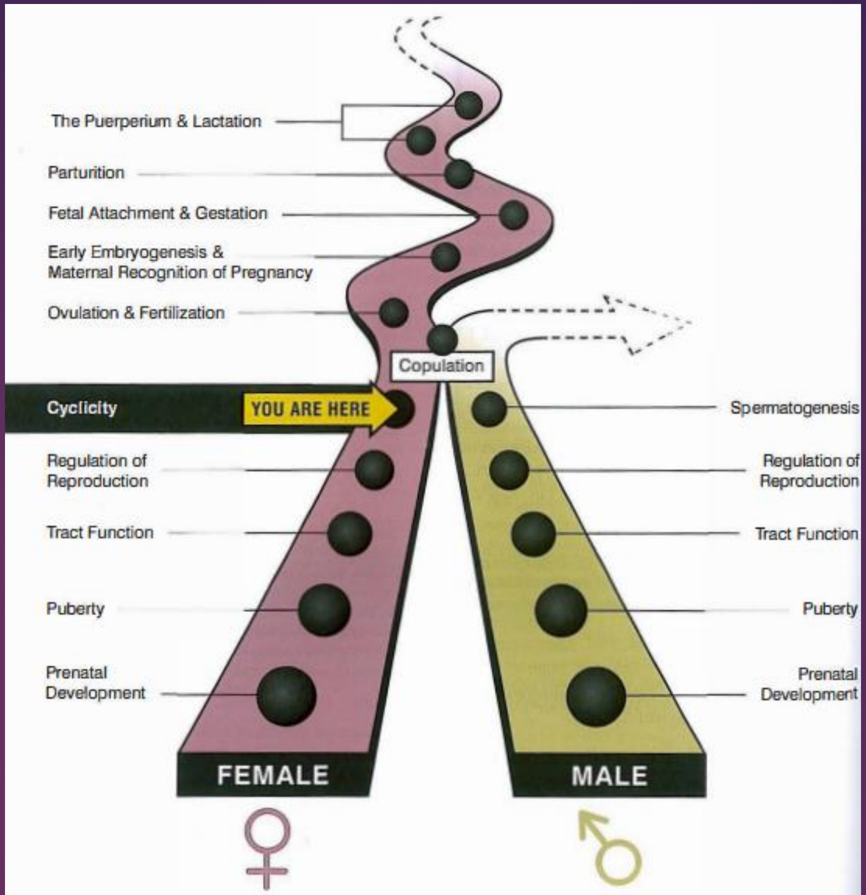

Section VII

Reproductive cyclicity

The Follicular Phase

The Follicular Phase

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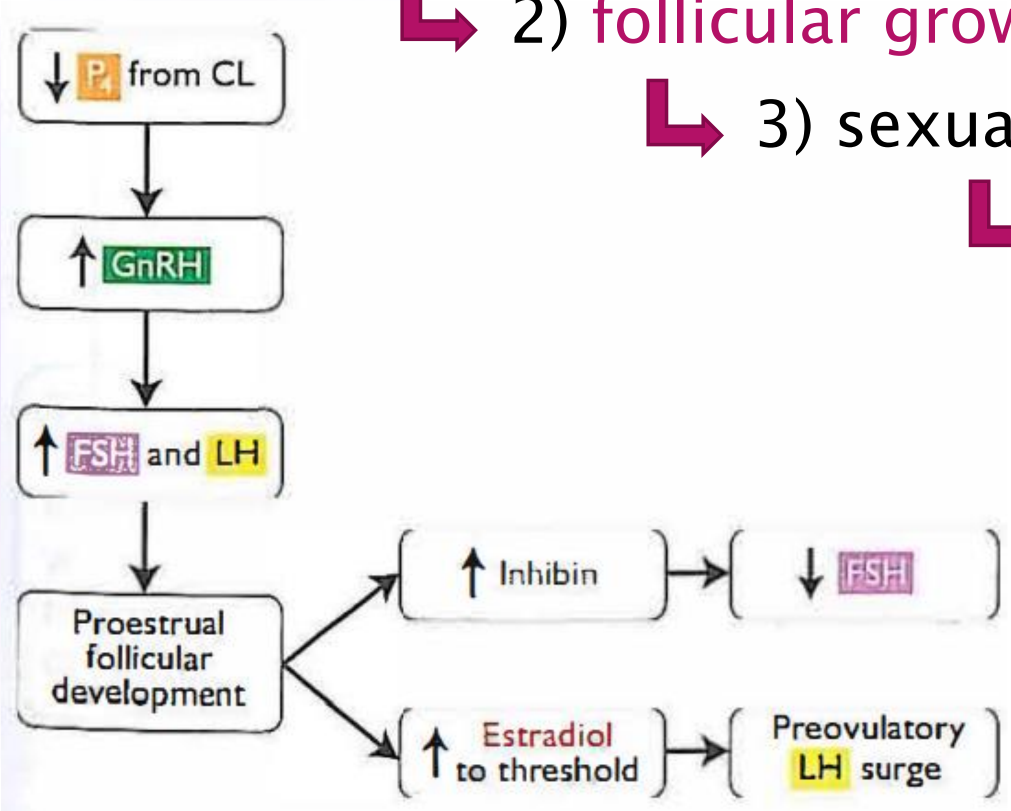
- The follicular phase consists of four major events.

1) elevated GnRH secretion from the AL of the pituitary after previous luteolysis

↳ 2) follicular growth and preparation for ovulation

↳ 3) sexual receptivity (estrus or heat)

↳ 4) ovulation



Hypothalamus-Pituitary-Ovary Axis

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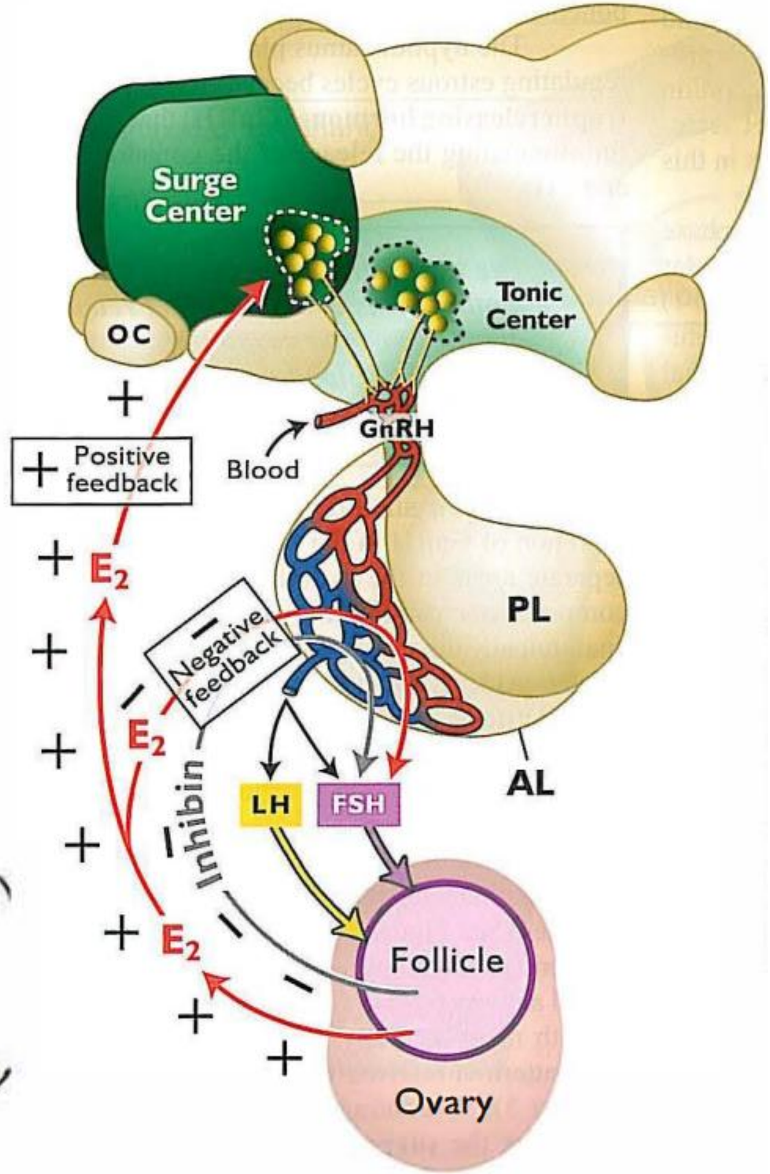

AL = Anterior Lobe
E_2 = Estradiol
OC = Optic Chiasm
PL = Posterior Lobe

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

Later in the follicular phase, follicles secrete inhibin that causes a negative feedback on FSH secretion from the anterior lobe of the pituitary. Estradiol is thought to suppress FSH secretion by the anterior lobe.

Tonic vs. Surge Secretion of GnRH

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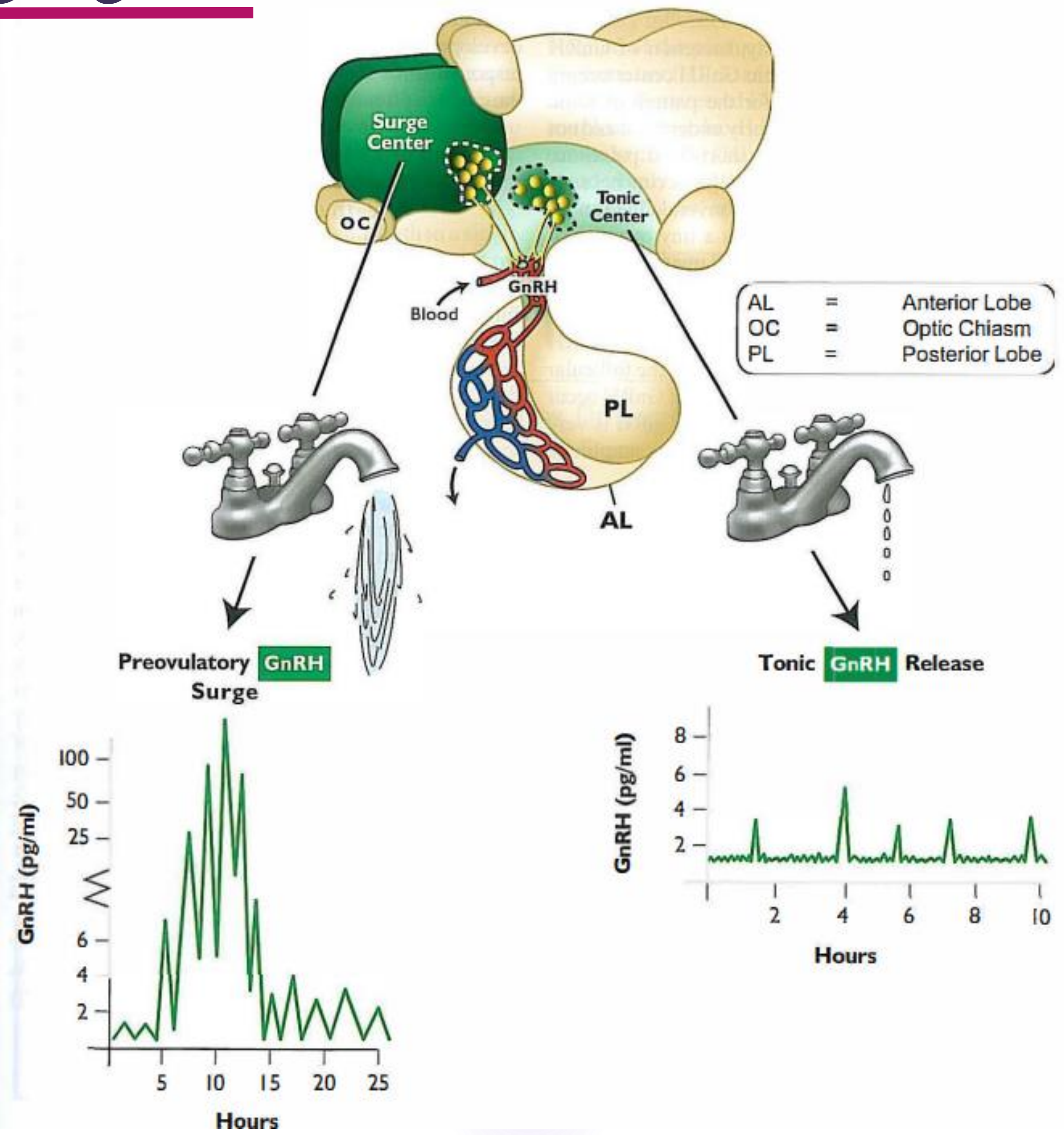
The surge center is sensitive to positive feedback and secretes high amplitude, high frequency pulses of GnRH (like a gushing, wide-opened faucet) in a relatively short period (hours) after estradiol reaches a threshold concentration.

The tonic center secretes small episodes of GnRH in a pulsatile fashion similar to a dripping faucet. The episodic secretion is continuous throughout reproductive life.



Hormonal Changes During the Follicular Phase

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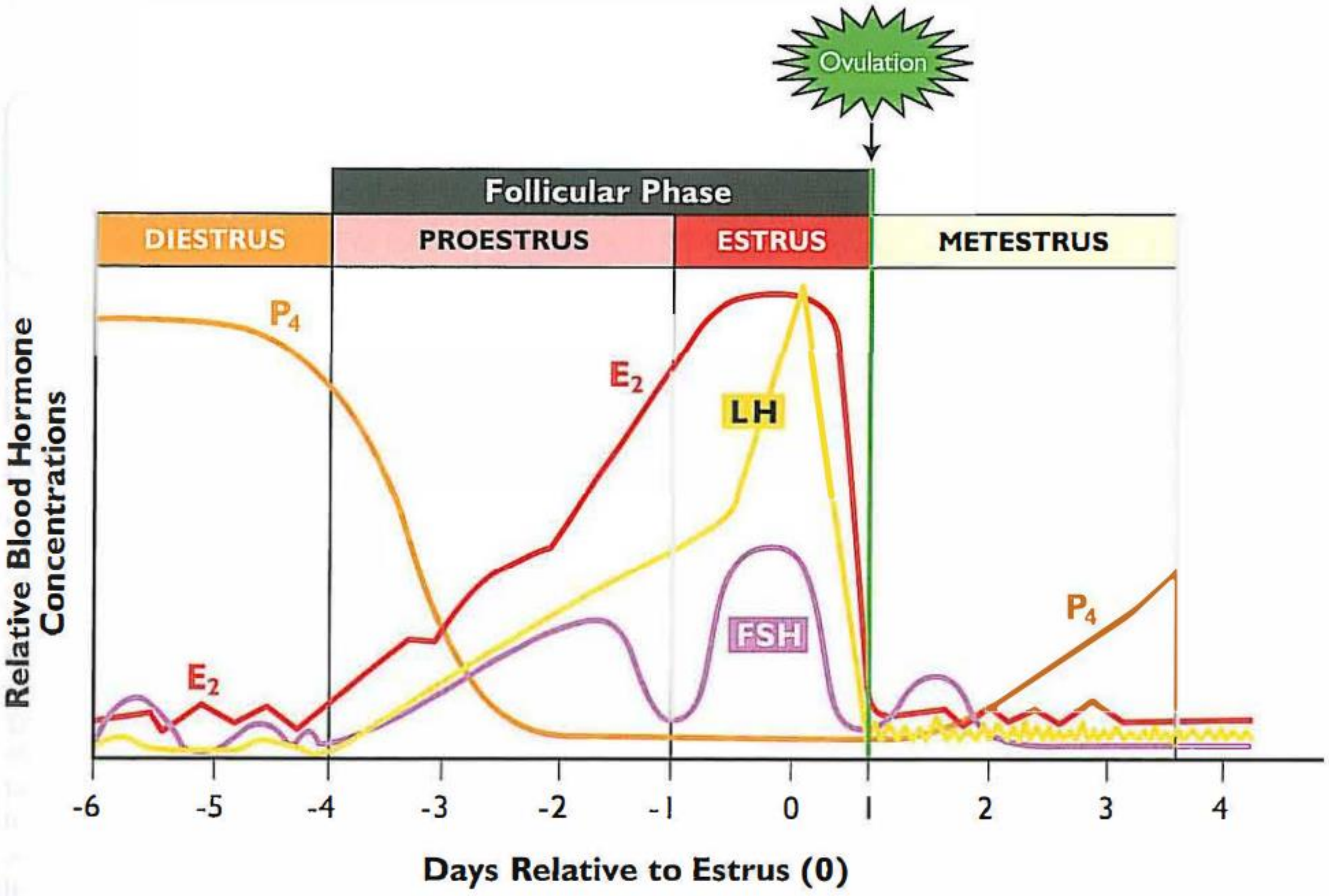
Proestrus

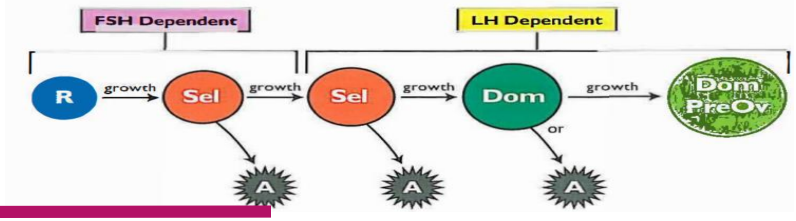
On day -6 (day 15) FSH surges to recruit the preovulatory wave, then FSH drops and remains low until it surges again with LH prior to ovulation.

Estrus

When recruited follicles develop dominance, they secrete 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 estradiol reaches a threshold concentration (peak), the preovulatory surge of LH occurs, inducing ovulation.



Follicular Dynamics



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- Even though the follicular phase comprises only about 20% of the estrous cycle, the process of follicular growth and degeneration (known as follicular dynamics) occurs continuously throughout the entire estrous cycle.
- The dynamics of antral follicles involve four processes:
  - Recruitment (or emergence): is the phase of follicular development in which a cohort (group) of small antral follicles begins to grow (emerge) and secrete estradiol.
  - Selection: Most of the recruited follicles undergo atresia. a group of growing follicles that have not undergone atresia are selected.
  - Dominance: one or more large preovulatory follicles exert a major inhibitory effect on other antral follicles by a combination of the production of inhibin and estradiol by the dominant follicle and reduced blood supply to some follicles.
  - Atresia: Suppressed FSH concentrations and reduced blood supply results in atresia.

Follicular Waves

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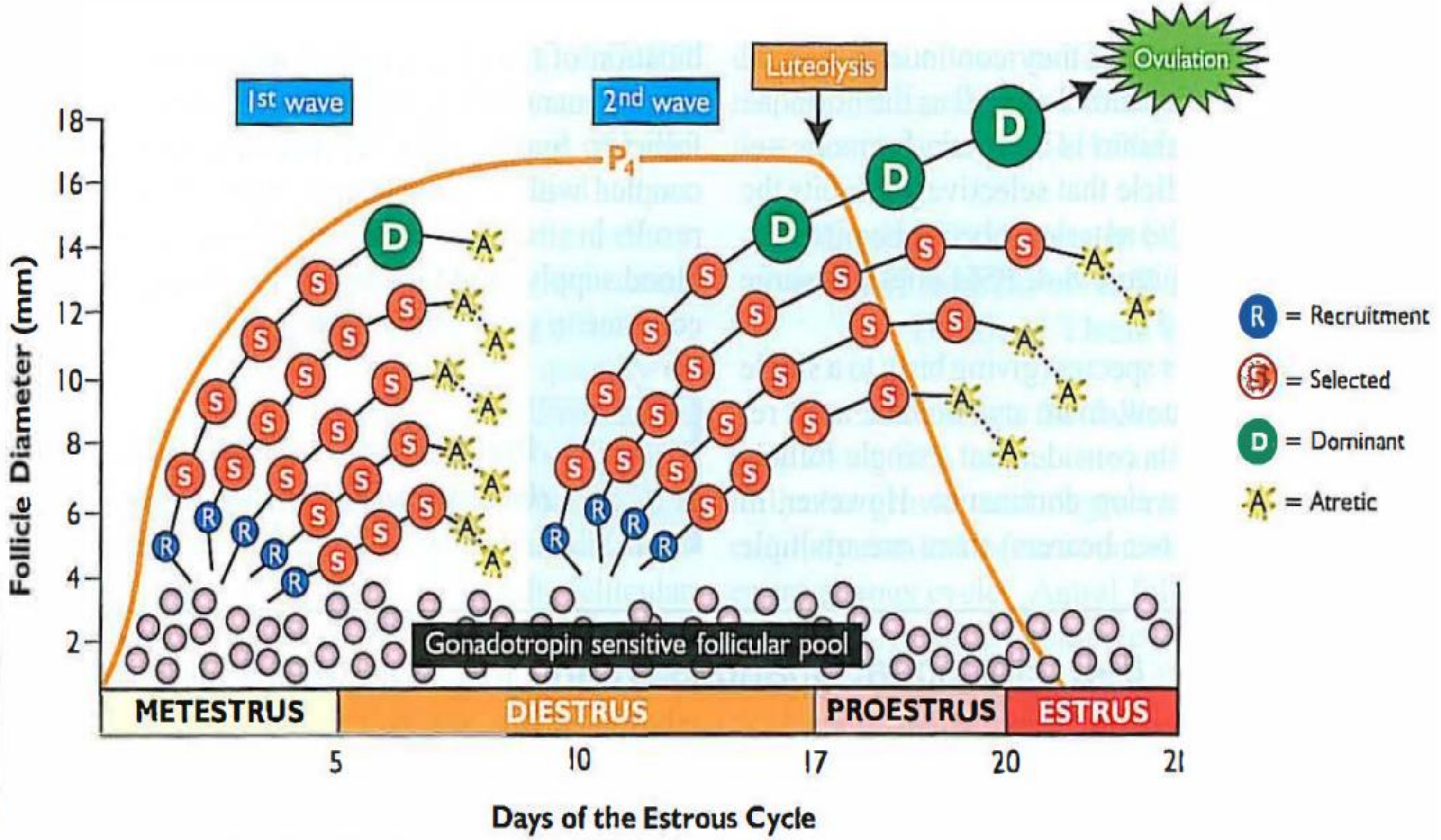
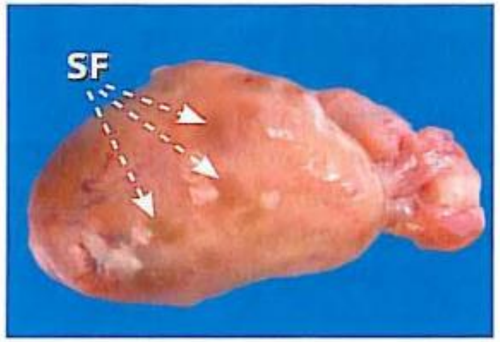
The first follicular wave occurs either as progesterone is rising or during peak progesterone secretion. Follicles recruited and selected during the first wave will become atretic. *Note: about 80% of estrous cycles in the cow have two waves, but some have three waves. This model illustrates a two-wave cycle.*

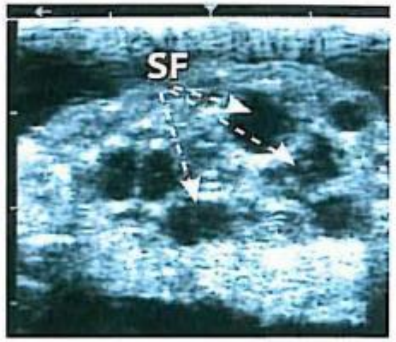
The second follicular wave is initiated before luteolysis and results in a dominant follicle that will ovulate. Only those follicles in a growing phase when luteolysis occurs will become eligible for ovulation.



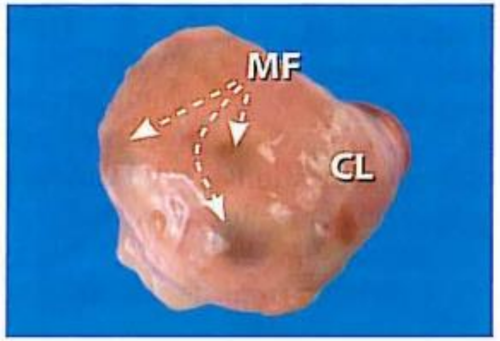
The Ovarian Follicle Diagnosis by US

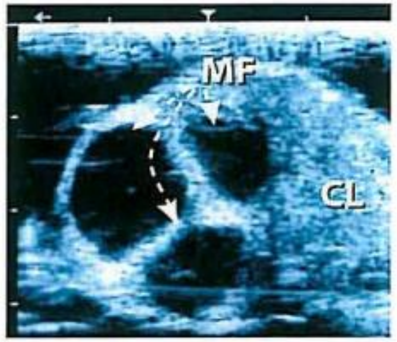
This ovary contains many small antral follicles (SF). More follicles appear in the ultrasonographic image than appear in the photograph because ultrasound imaging allows observation of follicles beneath the surface of the ovary. Fluid-filled cavities generate a black image while dense tissue like the ovarian stroma (OS) generates a gray to white image.



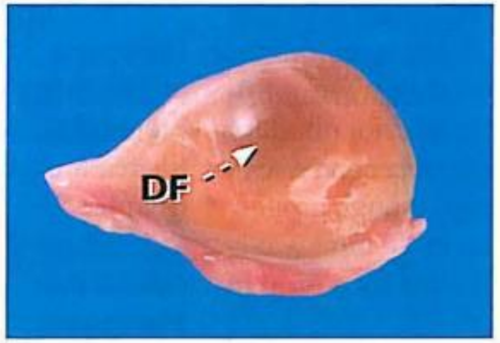


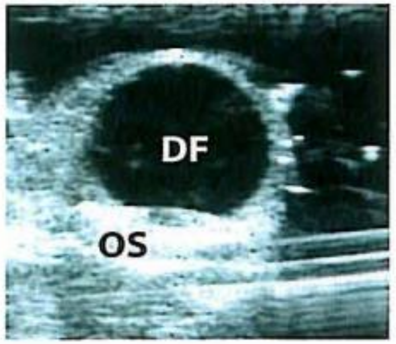
This ovary contains three medium antral follicles (MF) and a corpus luteum (CL) that appear in both images.





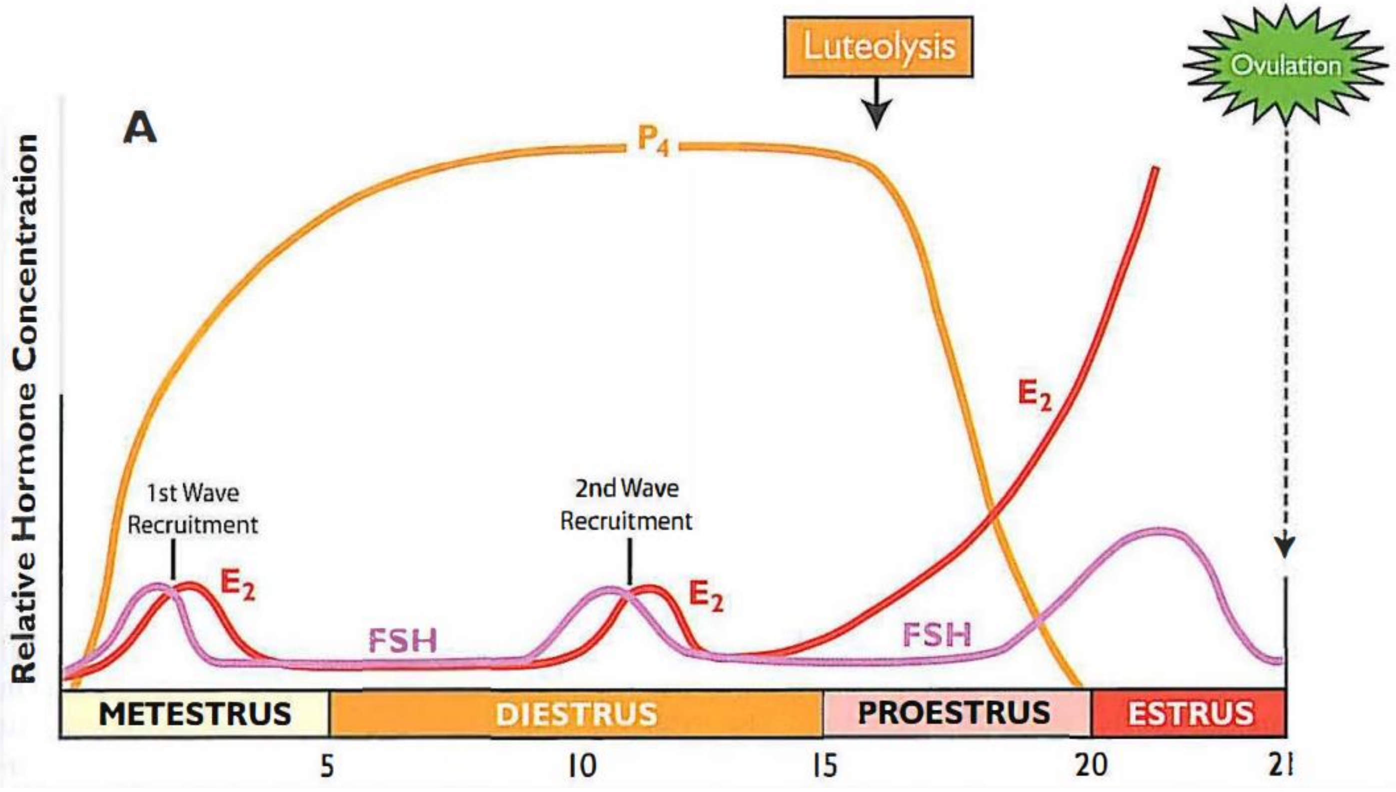
This ovary contains a dominant follicle (DF). The ultrasonogram shows that the follicle penetrates deep into the center of the ovary. This follicle could easily be palpated per rectum. However, the exact size of the follicle would be difficult to ascertain. Ultrasound technology allows changes in diameter to be measured precisely.





FSH, LH, P4 and E2 Secretions in Estrous Cycle

- FSH secretion followed by estradiol secretion occurs during metestrus even though progesterone is high.
- Antral follicles secrete estradiol in response to FSH. They also secrete inhibin and this causes FSH secretion to drop.
- After luteolysis, progesterone decreases. As a consequence, FSH and estradiol increase dramatically. FSH secretion is controlled by inhibin and estradiol.



FSH, LH, P4 and E2 Secretions in Estrous Cycle

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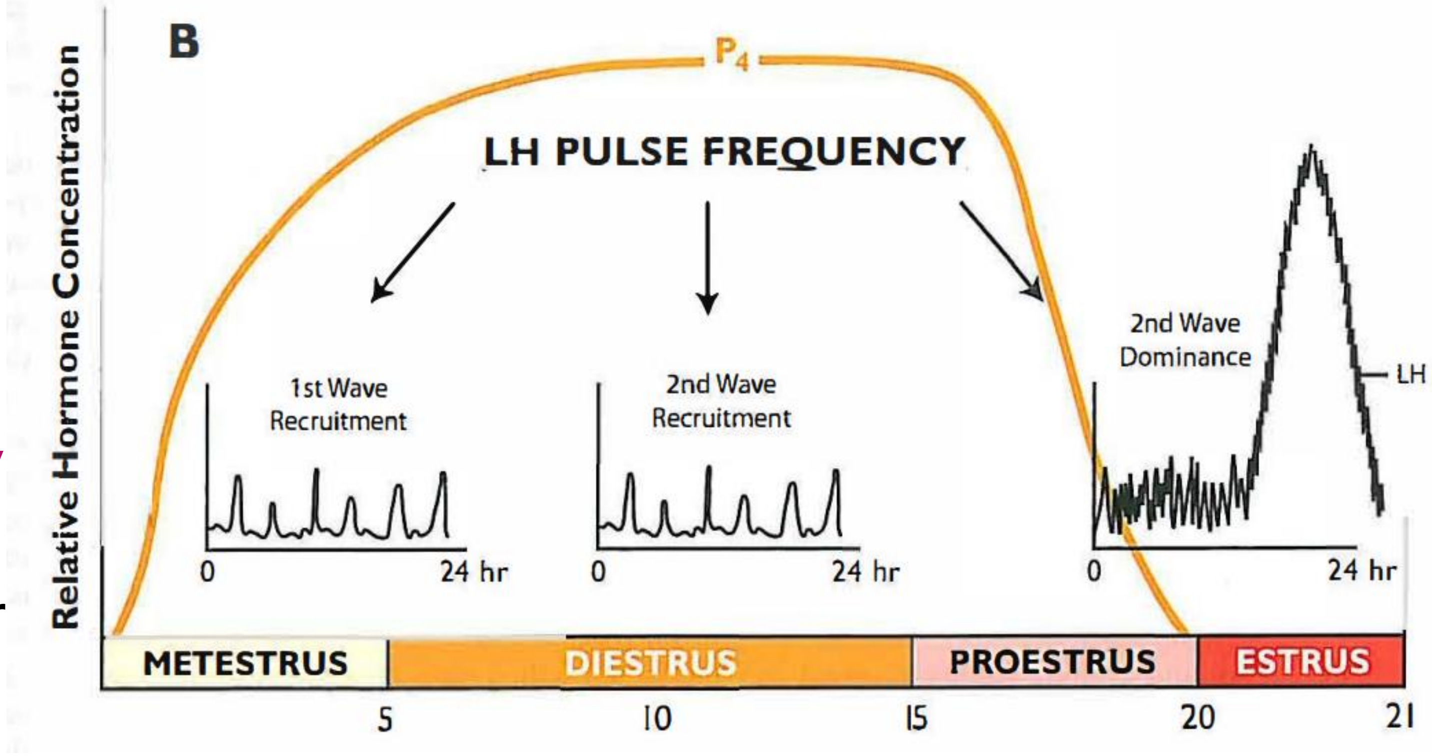
- Pulse frequency is low during metestrus (6 pulses per day) and diestrus (3 pulses per day).
- After luteolysis, progesterone secretion decreases and the negative feedback on GnRH is lifted and the pulse frequency for LH increases dramatically to about one pulse every hour
- This frequent pulses of LH drives final follicular development and ovulation



Roles of FSH and LH in Follicular Dynamics

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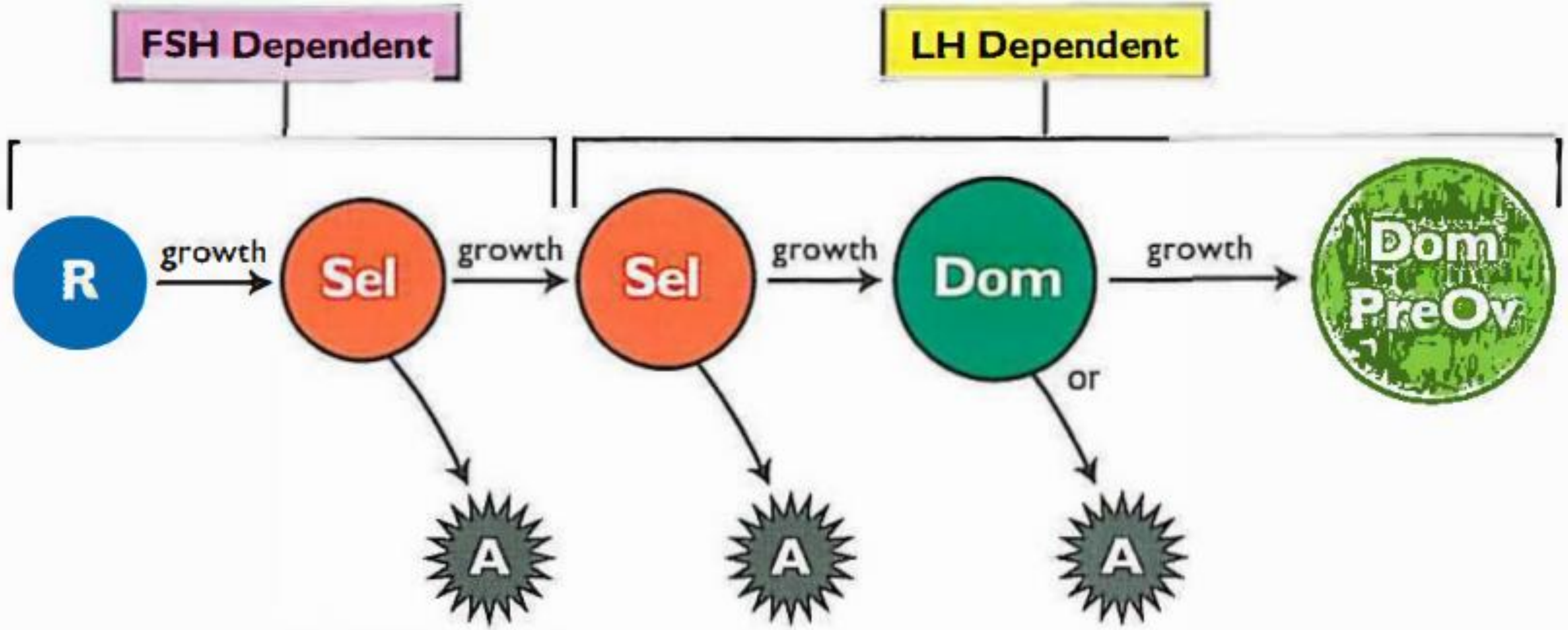
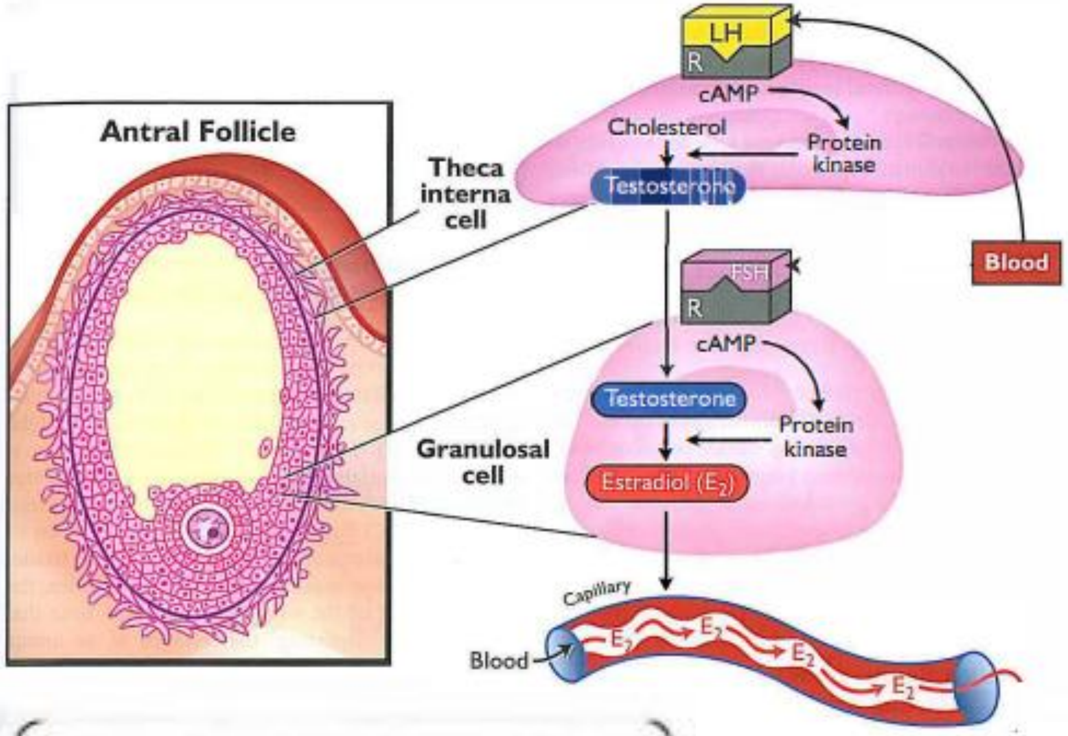
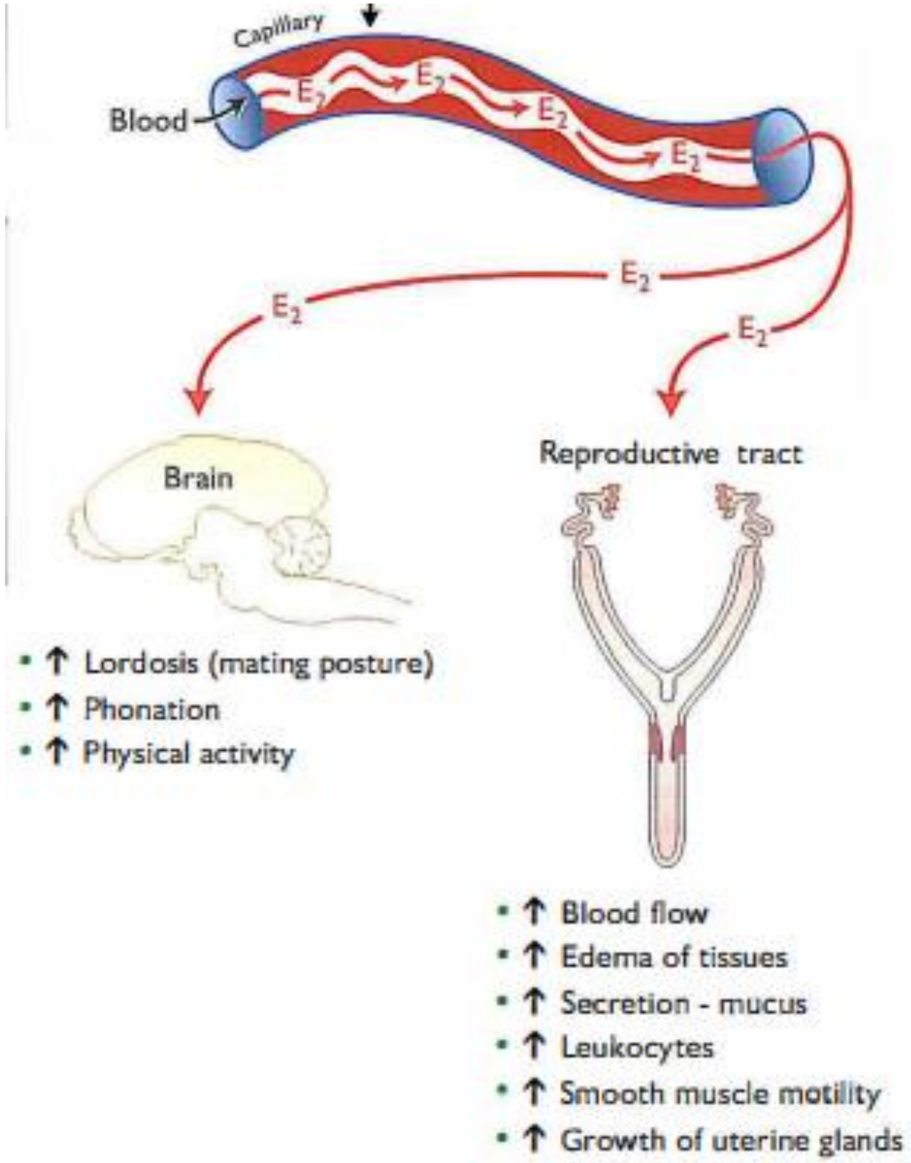


Emerging or recruited follicles and early selected follicles are predominantly FSH dependent. Larger selected follicles and dominant follicles are predominantly LH dependent. Follicles with high numbers of LH receptors become preovulatory follicles.

The Major Effects of Estradiol on the Reproductive Tract VII



The cells of the theca interna contain receptors for LH. Thecal cells produce testosterone that diffuses into the granulosal cells that contain FSH receptors. Binding of FSH to the granulosal cell receptors causes the synthesis of enzymes that are responsible for the conversion of testosterone to estradiol.

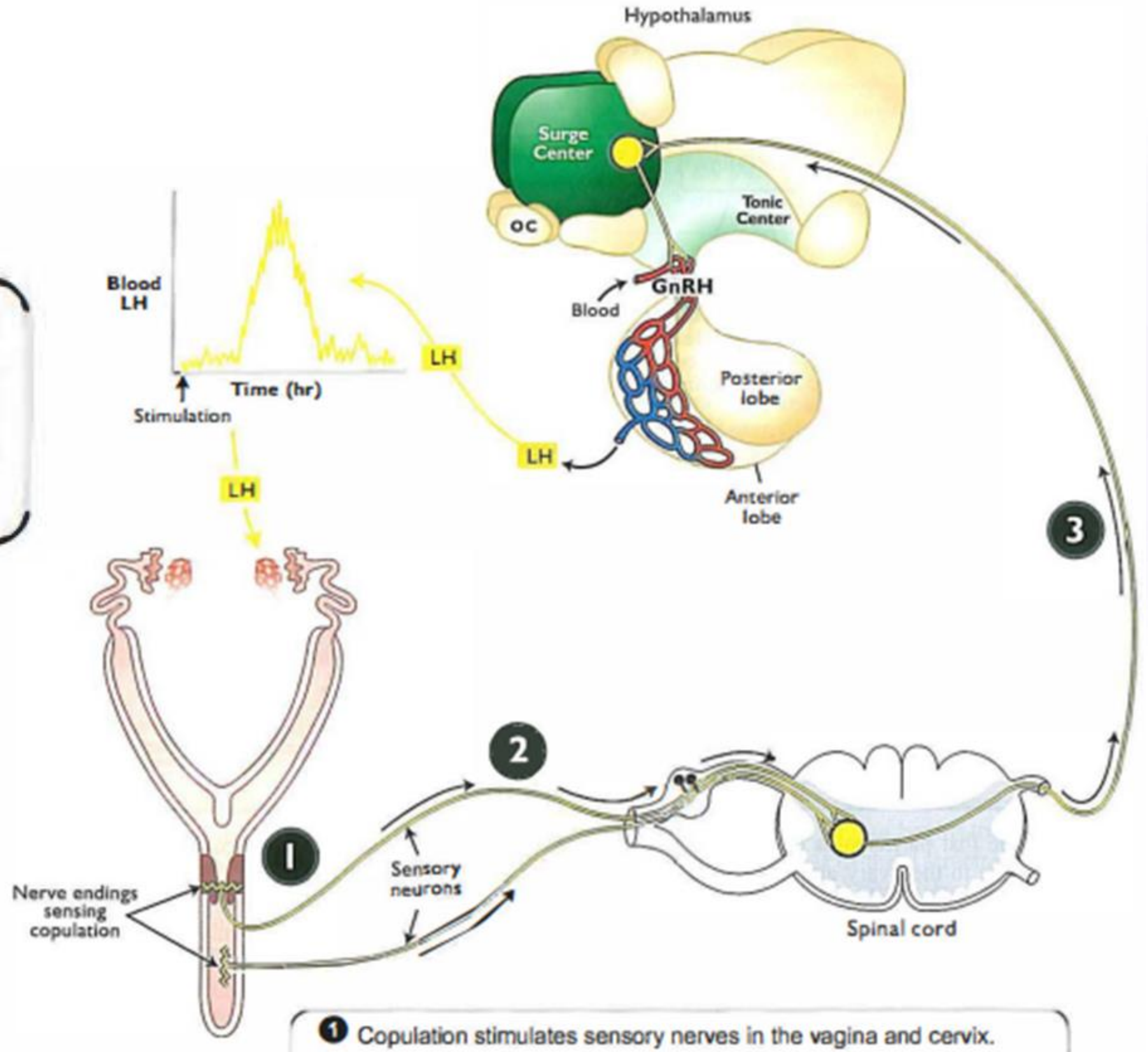


Induced Ovulation

- Among mammals there are two types of ovulators:
  - Spontaneous ovulators: ovulate with a regular frequency and do not require copulation. ovulation is brought about totally in response to hormonal changes.
    - Examples of spontaneous ovulators are the cow, sow, ewe, mare and the woman.
  - Reflex (induced) ovulator requires stimulation of the vagina and/or cervix for ovulation to occur.
    - Examples of reflex ovulators are the rabbit, felids, the ferret and the mink.
    - With the exception of the rabbit, induced ovulators have a relatively long copulation time (Camelids; 1 hr.) or copulate with intense frequency (over 100 times per estrus in lions).

Induced Ovulation

If sufficient stimulus is provided, neurons in the preovulatory center fire, causing large quantities of GnRH to be secreted that in turn stimulates the LH surge.



1. Copulation stimulates sensory nerves in the vagina and cervix.
2. Impulses are then relayed to the spinal cord.
3. Impulses are then relayed to the surge center in the hypothalamus.

The Major Steps of Oogenesis

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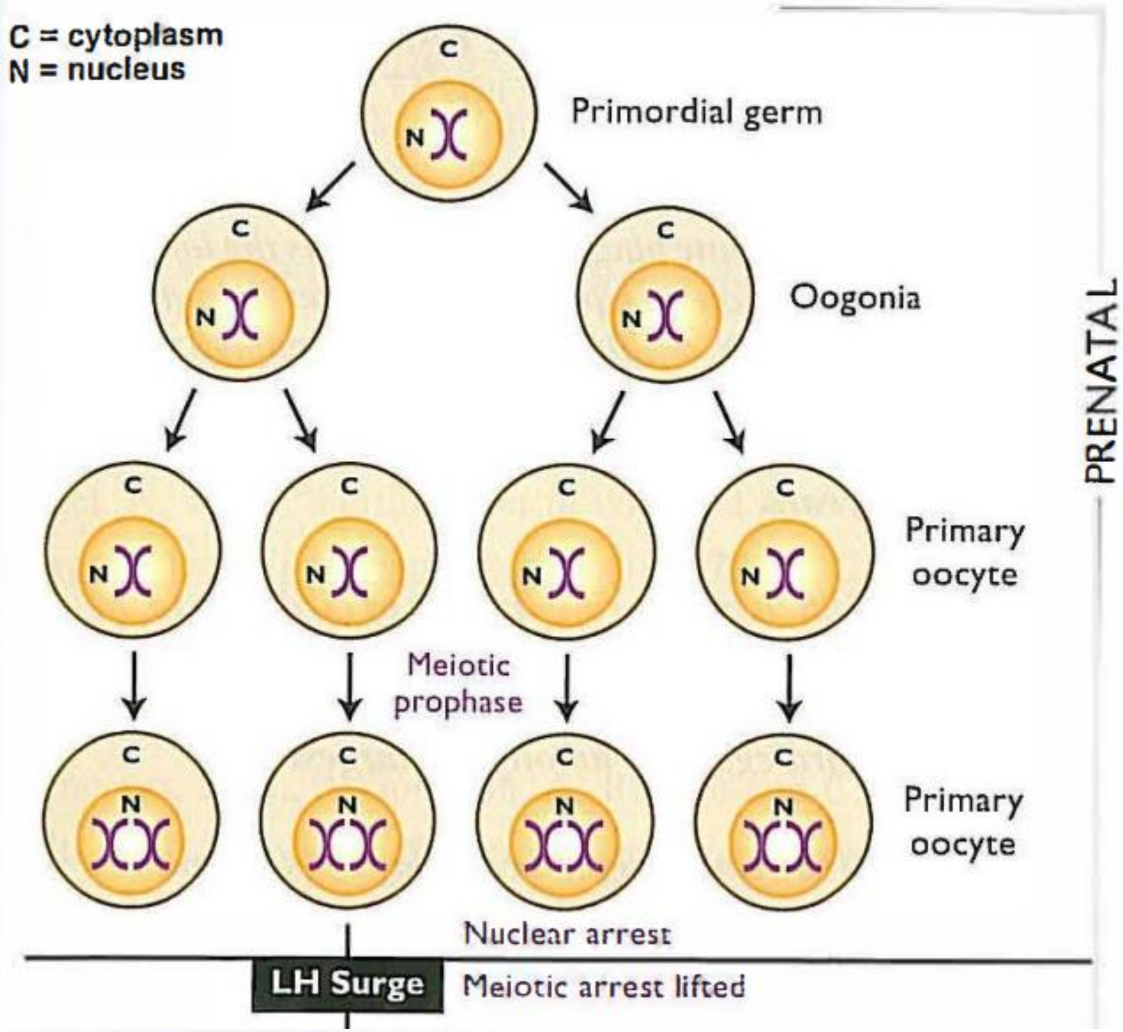

Prenatal

Oogenesis begins with the development of primordial germ cells in the embryo. Primordial germ cells divided mitotically into oogonia. Oogonia divided into primary ooyctes that enter the first meiotic prophase. At the end of meiotic prophase the nuclear material is arrested. This arrest is called the dictyate, a form of nuclear "hibernation".

The Major Steps of Oogenesis

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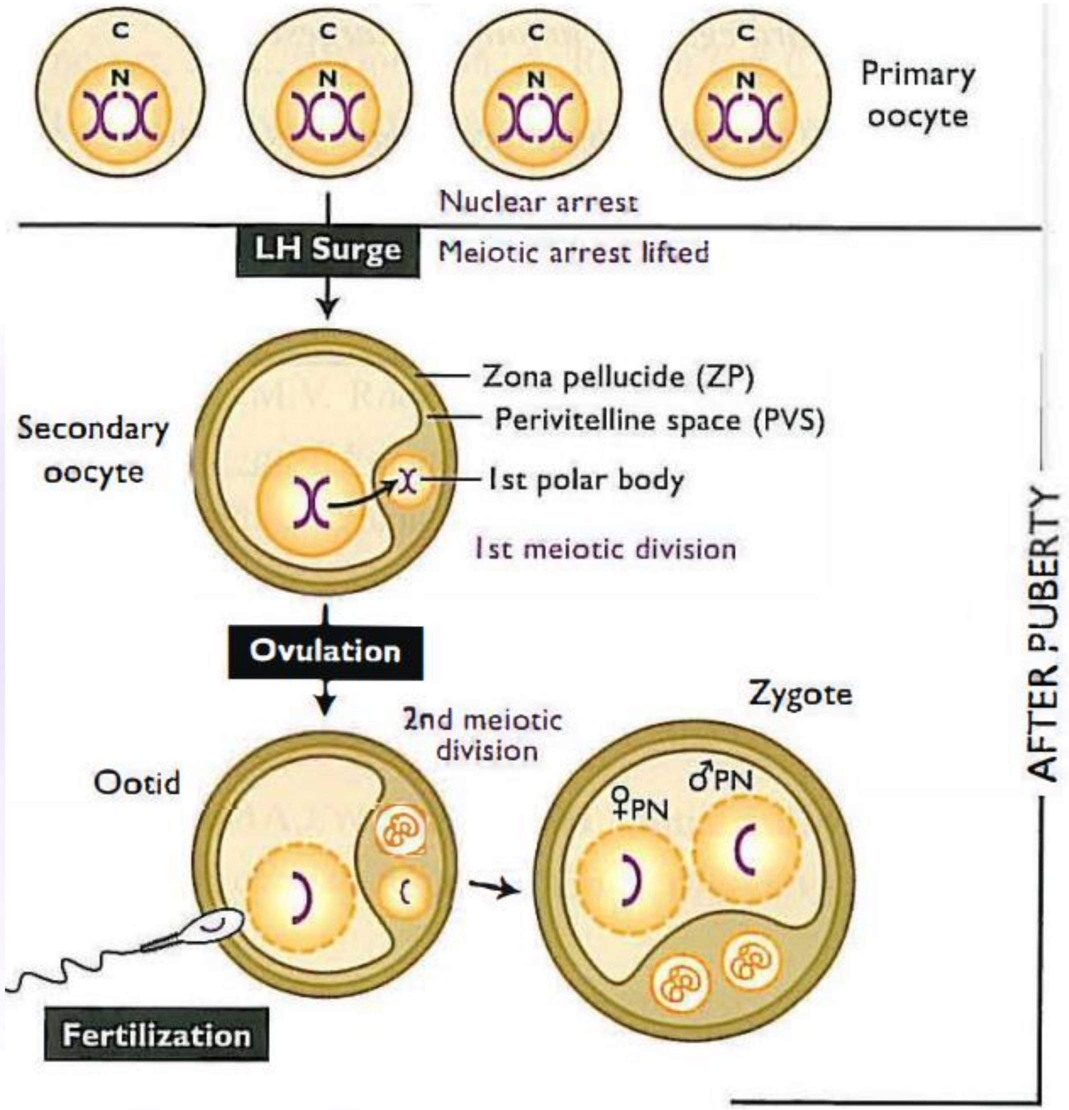
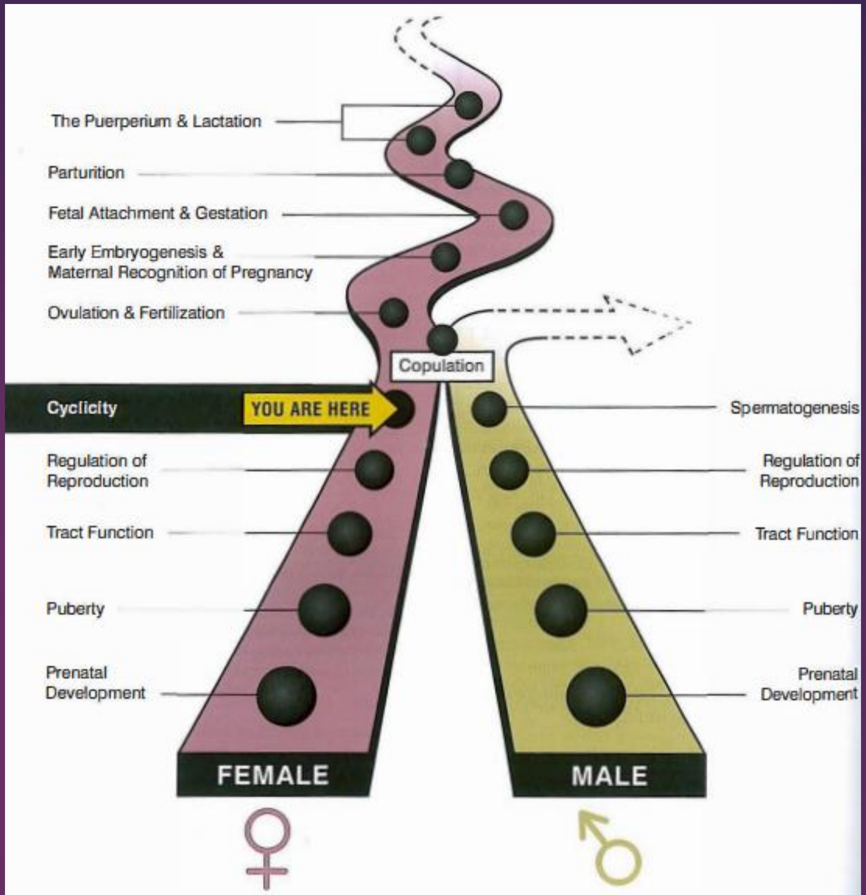


After Puberty

At puberty, the female begins to cycle and ovulate. The LH surge allows the meiotic arrest to be lifted in the first meiotic division takes place. This division results in the formation of a secondary ooycte that possesses the first polar body. The first polar body contains one-half of the genetic material. Around the time of ovulation, the second polar body is voided and the ootid is formed. Fertilization occurs slightly before or slightly after the second meiotic division. At fertilization the sperm delivers the other half of the genetic material and a zygote is formed. At this time the zygote contains a male and a female pronucleus. When the pronucleii fuse, early embryo development begins.



Section VIII

Reproductive cyclicity

The Luteal Phase

The Luteal Phase

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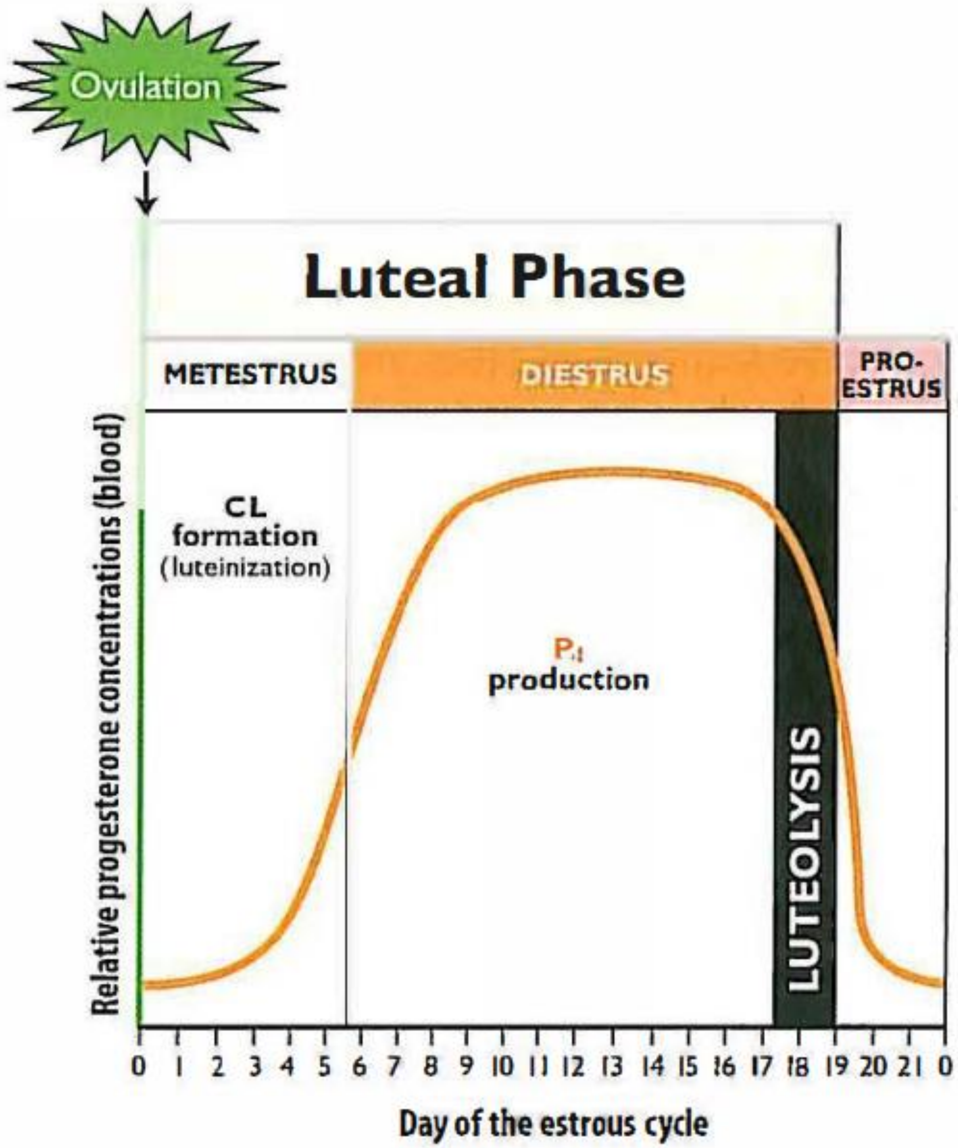
The luteal phase begins immediately after ovulation. During the early luteal phase, the corpus luteum (CL) develops (luteinization) and progesterone increases. During the mid-luteal phase (diestrus) the corpus luteum is fully functional and progesterone (P_4) plateaus. During the last 2-3 days of the luteal phase, destruction of the corpus luteum occurs (luteolysis) and the luteal phase terminates. Following luteolysis, proestrus is initiated.



Formation of the Corpus Luteum

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- After ovulation the theca interna and the granulosal cells of the follicle undergo a dramatic transformation known as luteinization.
- Luteinization is the process whereby cells of the ovulatory follicle are transformed into luteal tissue. This transformation is governed by LH.
- Shortly before ovulation the basement membrane of the follicle undergoes partial disintegration and the physical separation of the thecal and granulosal cells disappears.
- During ovulation, follicular fluid leaks from the follicle and then the wall of the follicle collapses forming many folds which mix thecal cells and the granulosal cells, thus forming a gland (CL).
- An exception to this is found in the corpora lutea of the woman and other primates, where thecal and granulosal cells are clustered into distinct "islets“.

Formation of the Corpus Luteum

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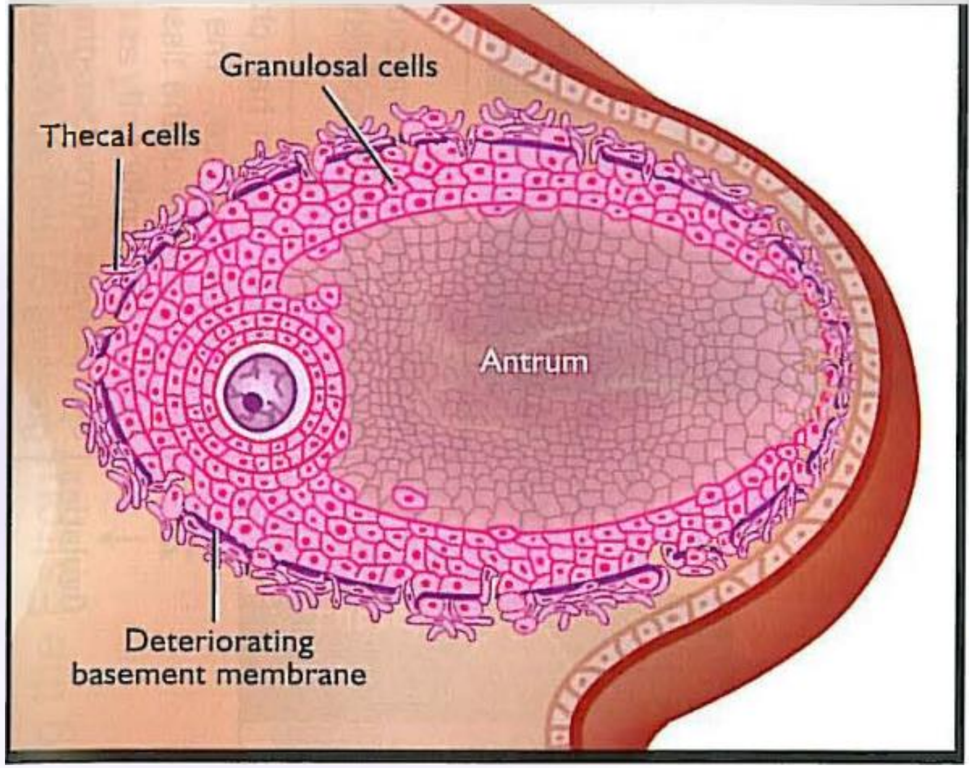

Preovulatory Follicle

The preovulatory follicle consists of granulosal cells that line the antrum. The basement membrane, separating the granulosal cells from the cells of the theca interna begins to deteriorate prior to ovulation because of the action of collagenase. Complete separation between the granulosal cells and the theca interna no longer exists and the cells can begin to intermingle.

Formation of the Corpus Luteum

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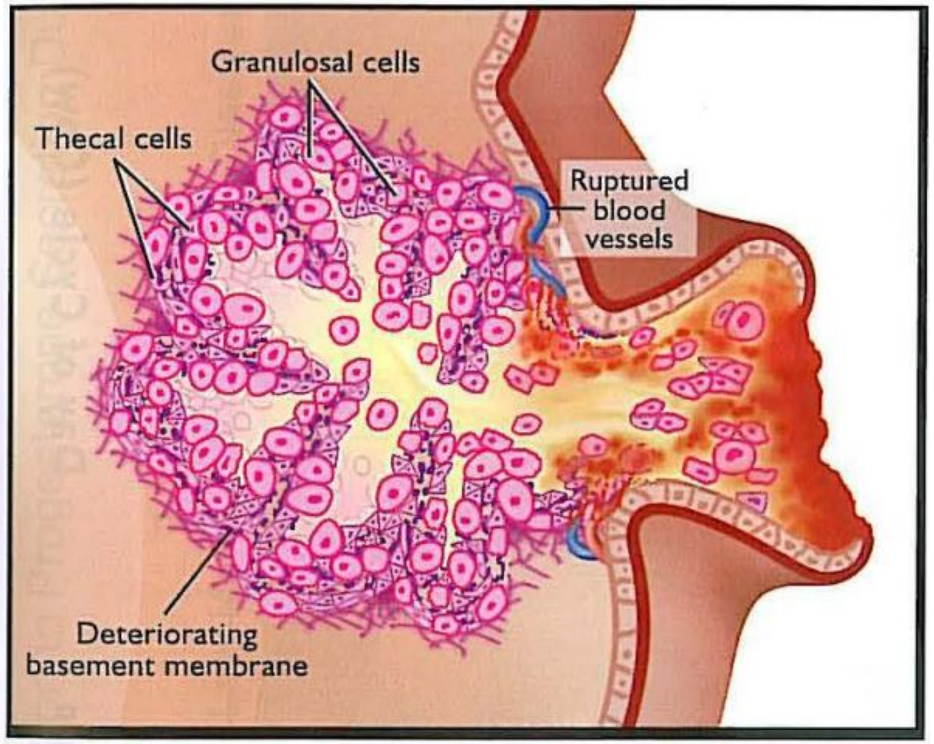
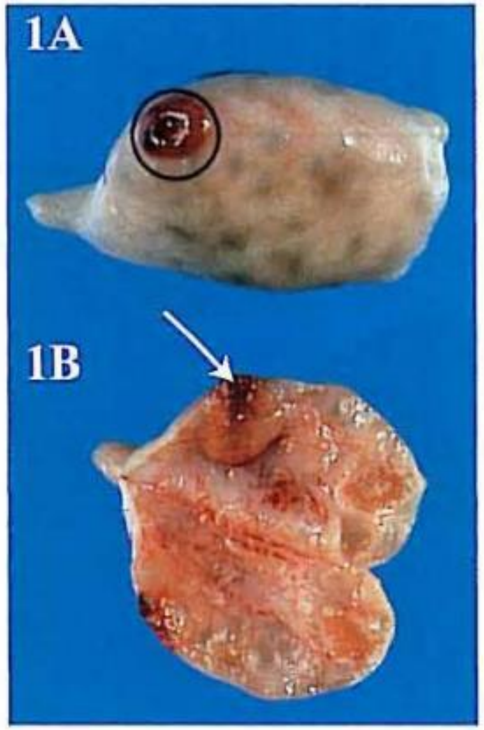


Corpus Hemorrhagicum (CH)

During ovulation, many small blood vessels rupture causing local hemorrhage. This hemorrhage appears as a blood clot on the surface of the ovary that sometimes penetrates into the center of the follicle after ovulation

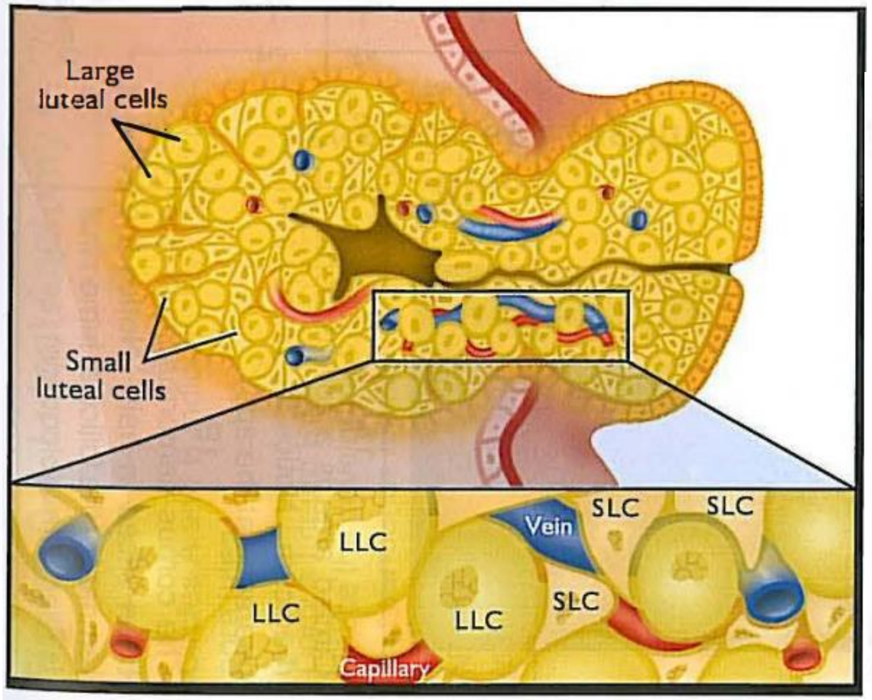
Following evacuation of the follicular fluid and oocyte, the follicle collapses into folds. The cells of the theca interna and the granulosa begin to mix. The basement membrane forms the connective tissue substructure of the corpus luteum.

Early Metestrus



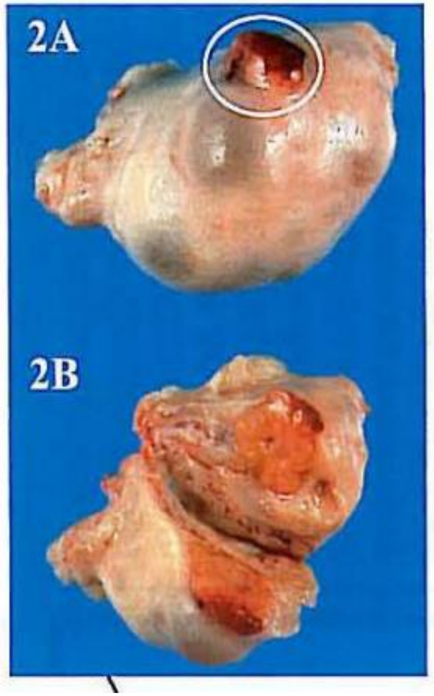
Formation of the Corpus Luteum

- Large luteal cells contain oxytocin in the corpus luteum of the cycle and are believed to contain relaxin in the corpus luteum of pregnancy.
- Small luteal cells do not contain secretory granules but like LLC can produce progesterone (P_4).
  - The use of real-time ultrasonography has proven effective for the examination of corpora lutea, as well as ovarian follicles.



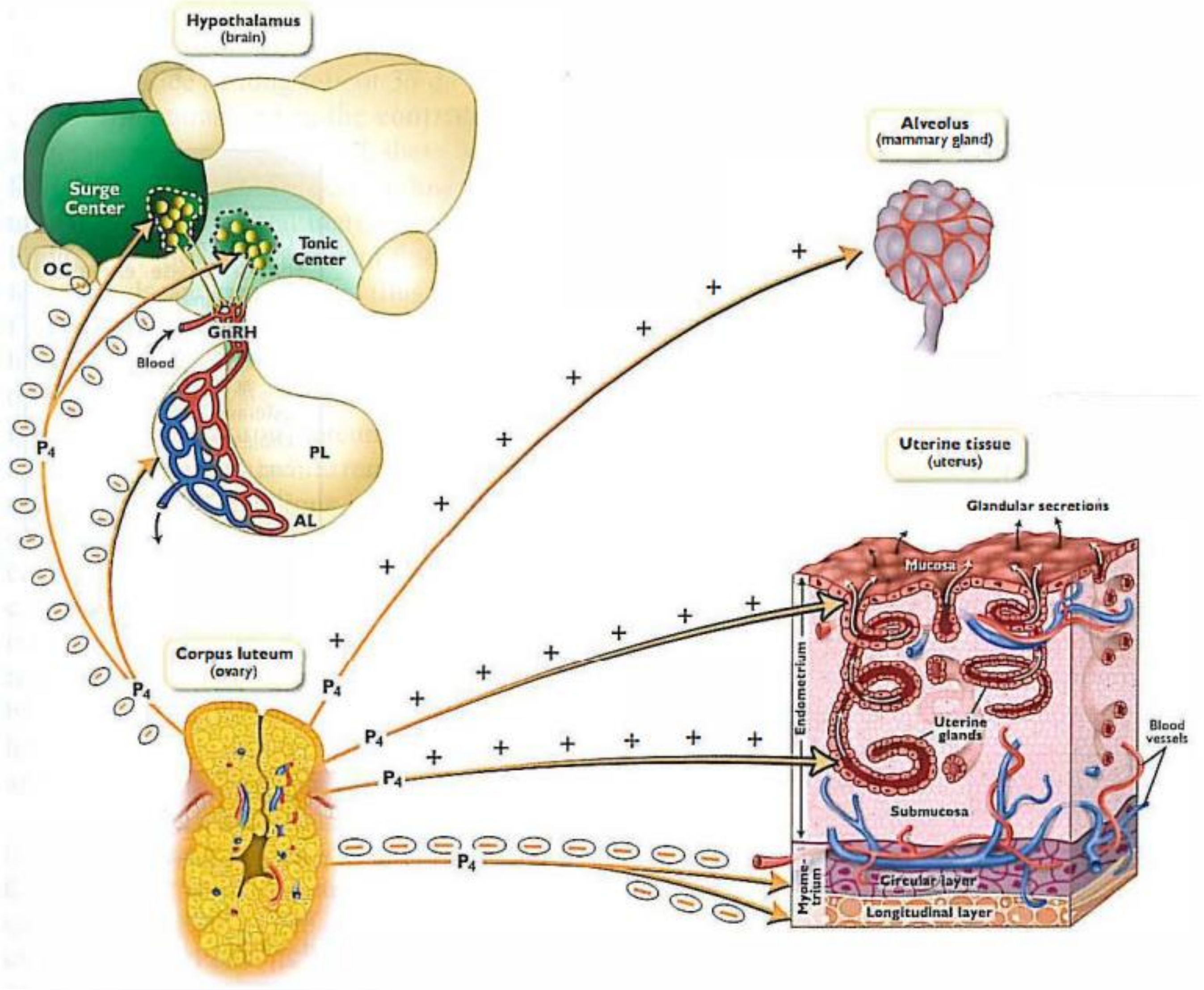
Functional Corpus Luteum (CL)
The corpus luteum is now a mixture of large luteal cells, LLC (formerly granulosal cells) and many small luteal cells, SLC (formerly thecal cells). In some cases, there is a remnant of the follicular antrum that forms a small cavity in the center of the corpus luteum

Late Metestrus



Progesterone (P_4) Physiological Effects

VIII

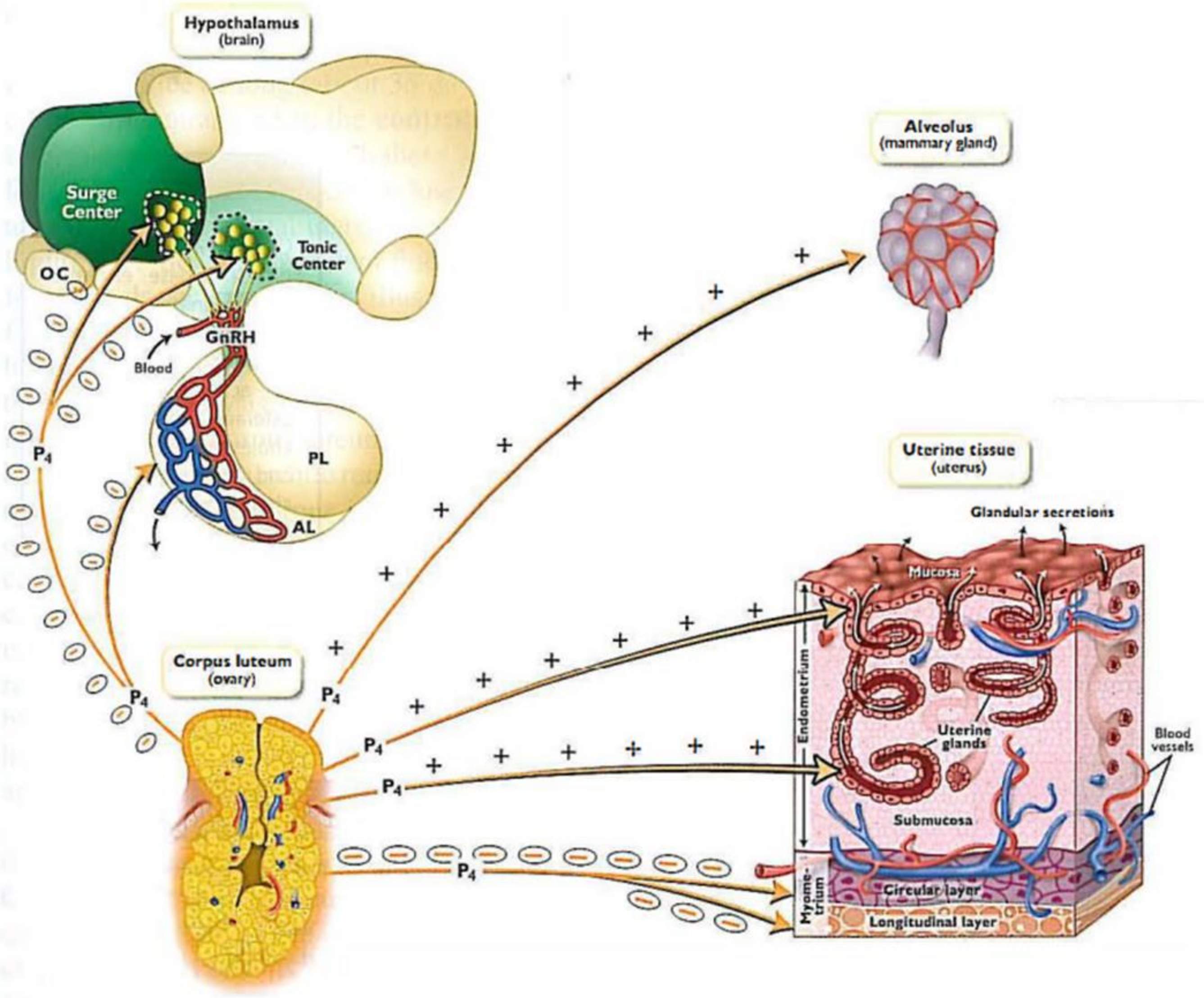


P_4 promotes alveolar development in the mammary gland, especially during pregnancy.

Progesterone (P_4) Physiological Effects

VIII

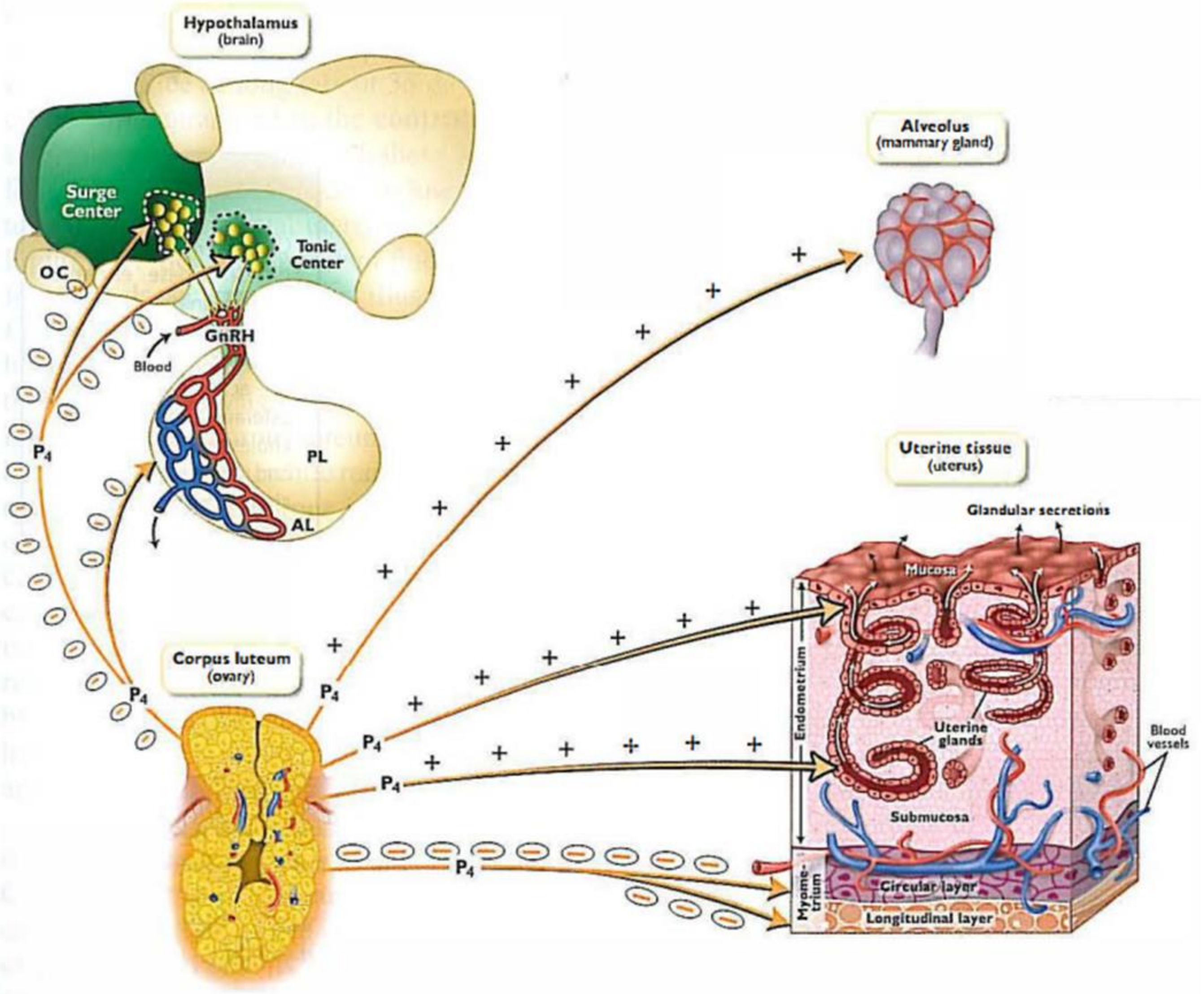
P_4 produced by the CL exerts a negative (-) feedback on the GnRH neurons of the hypothalamus. Therefore, GnRH, LH and FSH are suppressed and little estrogen is secreted. Progesterone is thought to decrease the number of GnRH receptors on the anterior pituitary.



Progesterone (P_4) Physiological Effects

VIII

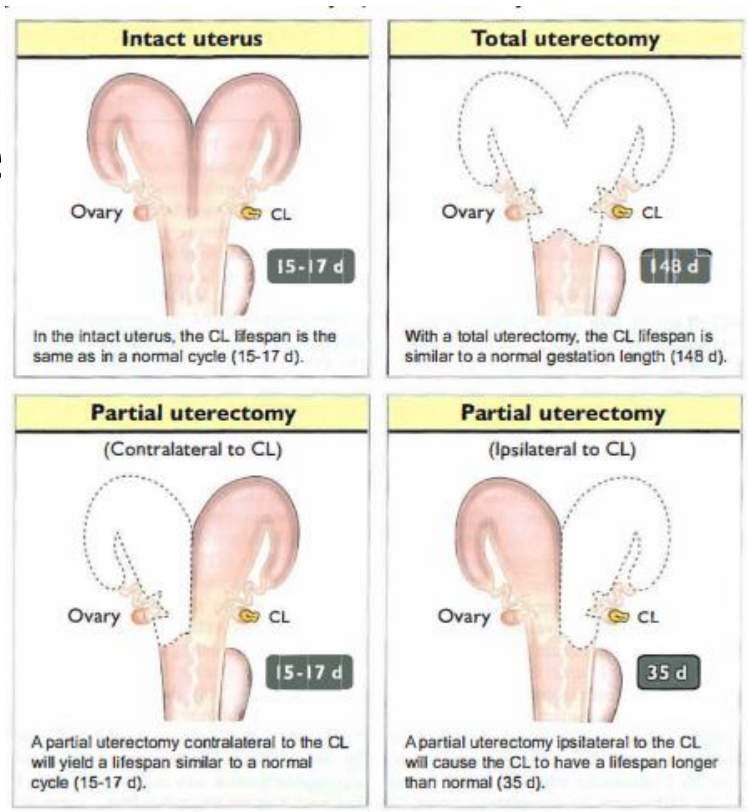
P_4 exerts a strong positive (+) influence on the endometrium of the uterus. Under the influence of P_4, the uterine glands secrete materials into the uterine lumen. Progesterone inhibits the myometrium and thus reduces its contractility and tone.

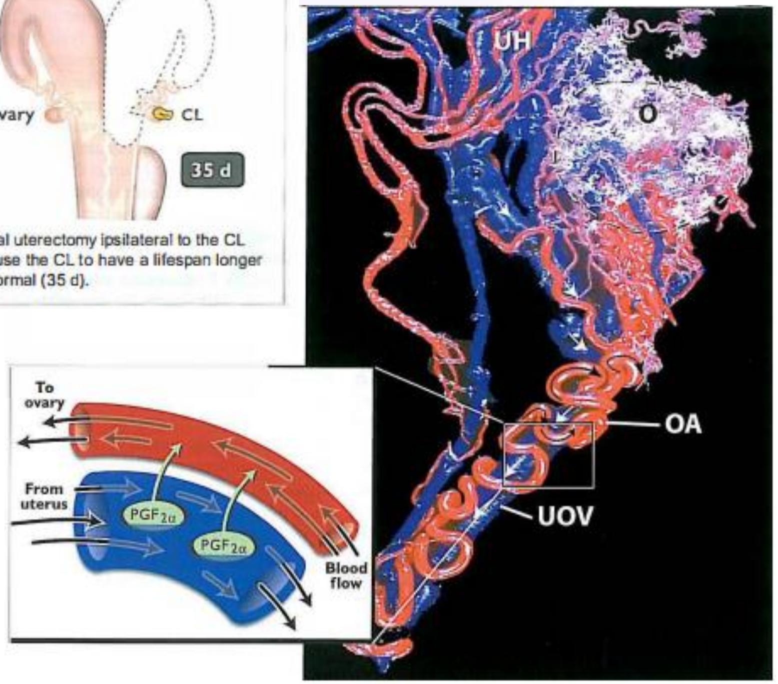


Luteolysis

VIII

- Luteolysis is a process whereby the corpus luteum undergoes irreversible degeneration characterized by a dramatic drop in blood concentrations of progesterone.
- The hormone inducing luteolysis is $PGF_{2\alpha}$ secreted by the uterine endometrium to the ipsilateral ovary through a vascular countercurrent exchange mechanism (except mare).
- This special anatomical relationship prevents the $PGF_{2\alpha}$ from dilution by the systemic circulation and be denatured in the pulmonary system.

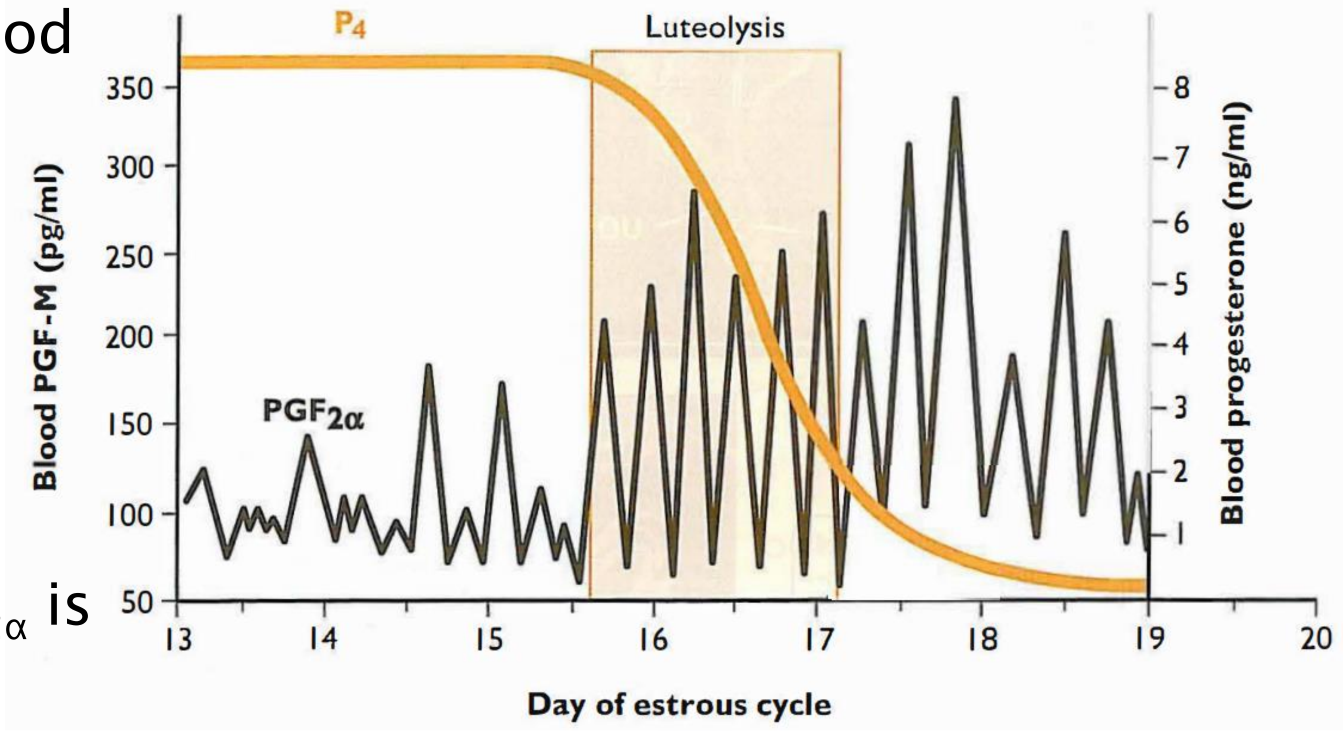




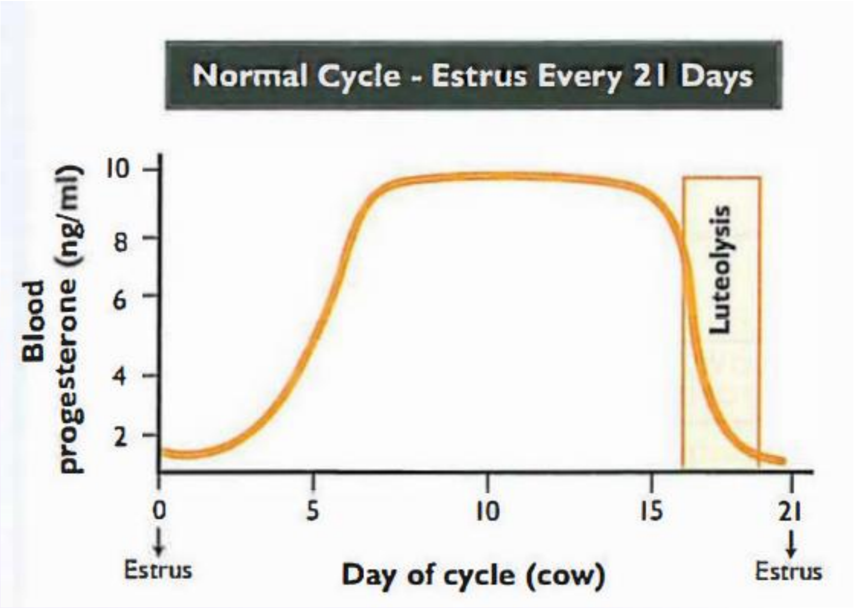
Luteolysis

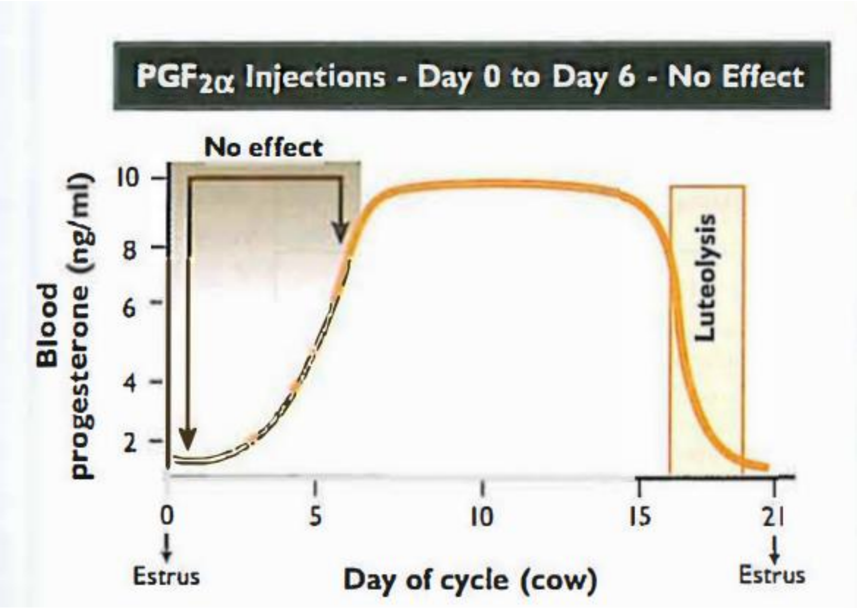
VIII

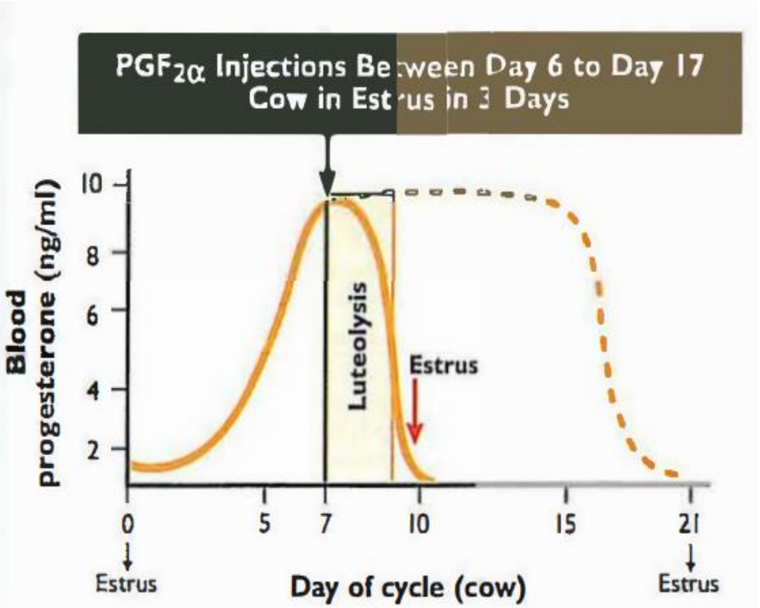
- A critical number of $PGF_{2\alpha}$ pulses within a given timespan are required to induce complete luteolysis
  - about five pulses in a 24 hour period are required in the ewe to induce complete luteolysis.
- Pulsatile release of $PGF_{2\alpha}$ is apparently not required under conditions of exogenous $PGF_{2\alpha}$ administration.
  - For example, one injection of $PGF_{2\alpha}$ is sufficient to cause luteolysis.



$PGF_{2\alpha}$ Injection and the Estrous Cycle



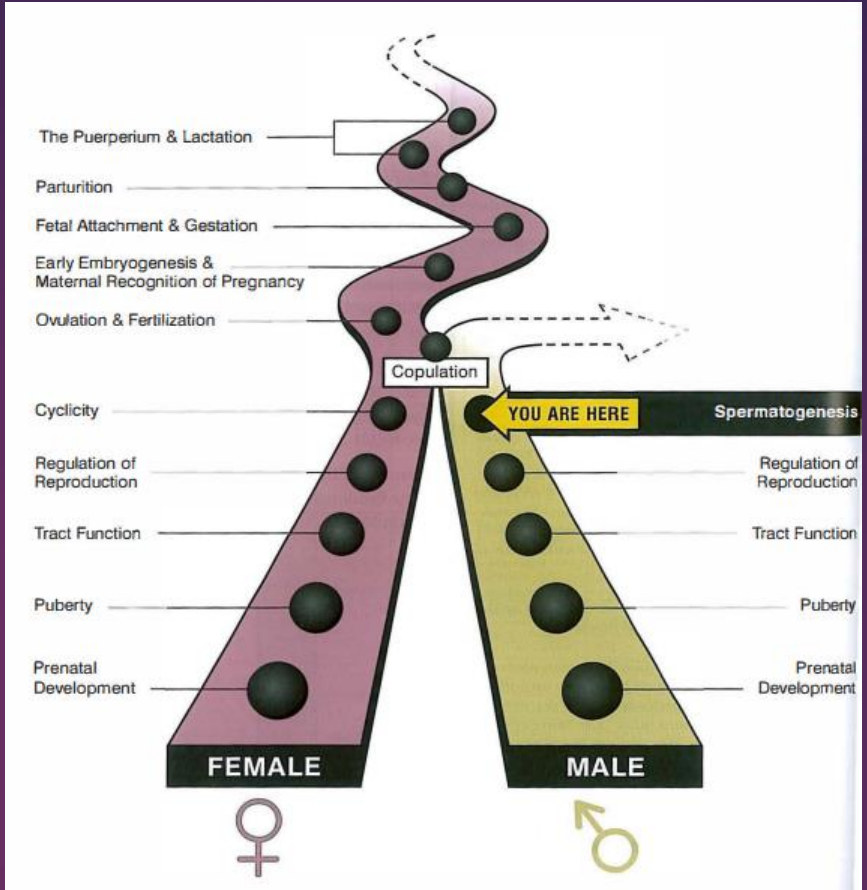




In the normal cyclic cow estrus and ovulation occurs every 21 days. Luteolysis (induced naturally by $PGF_{2\alpha}$ from the uterus) causes the animal to enter a new follicular phase and subsequent estrus.

If a single injection of $PGF_{2\alpha}$ is given between day zero and about day six, luteolysis will not occur and the cycle will be of normal length. This is because the corpus luteum must reach a certain stage of development before it is sensitive to $PGF_{2\alpha}$.

If $PGF_{2\alpha}$ is injected on day 7-17, luteolysis will occur. Progesterone will drop and the animal will come into estrus in about three days after the injection. Such a strategy is used to synchronize estrus in large groups of animals.



Section IX

Endocrinology of the male &

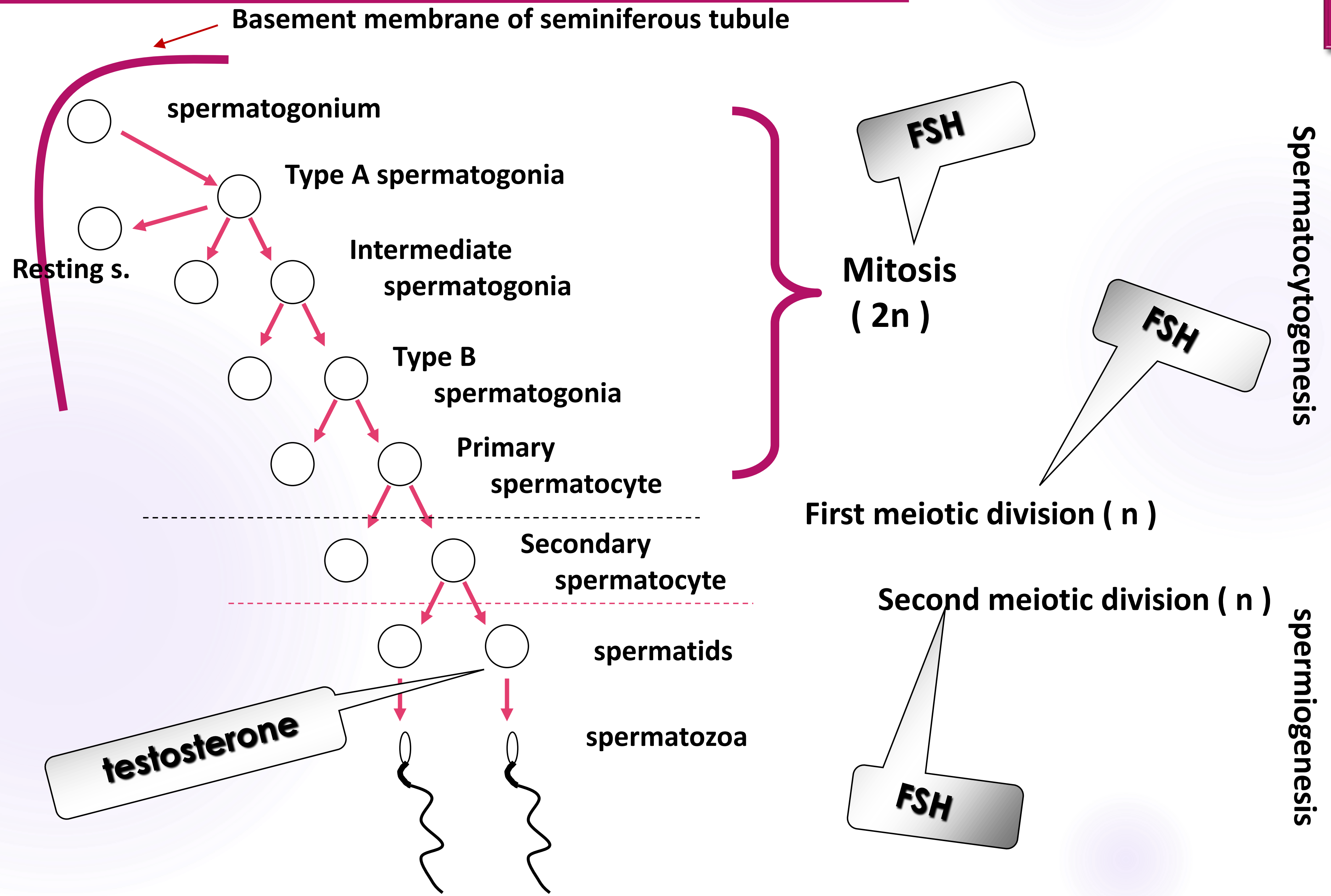
Spermatogenesis

Spermatogenesis

IX

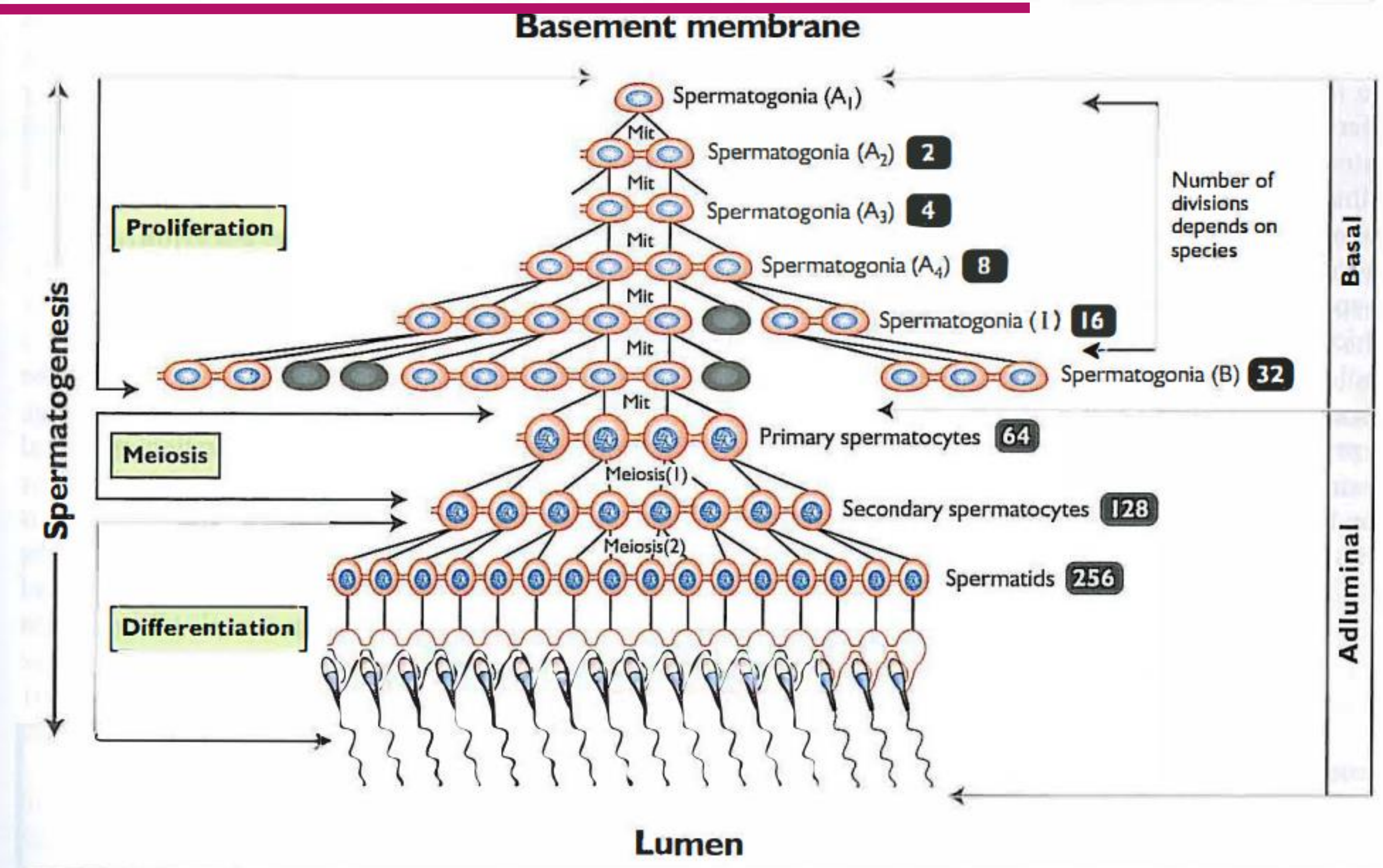
- Spermatogenesis takes place entirely within the seminiferous tubules and consists of all cell divisions and morphologic changes that occur to developing germ cells.
  - The proliferation phase, consists of all mitotic divisions of spermatogonia. Several generations of A-spermatogonia undergo mitotic divisions, generating a large number of B-spermatogonia
    - stem cell renewal is the reversion of some spermatogonia to stem cells
  - The meiotic phase begins with primary spermatocytes. During meiosis I, genetic diversity is guaranteed by DNA replication and crossing over during the production of secondary spermatocytes.
  - The differentiation phase in which a spherical undifferentiated spermatid undergoes a remarkable transformation that results in the production of a spermatozoon.

Spermatogenesis



Spermatogenesis

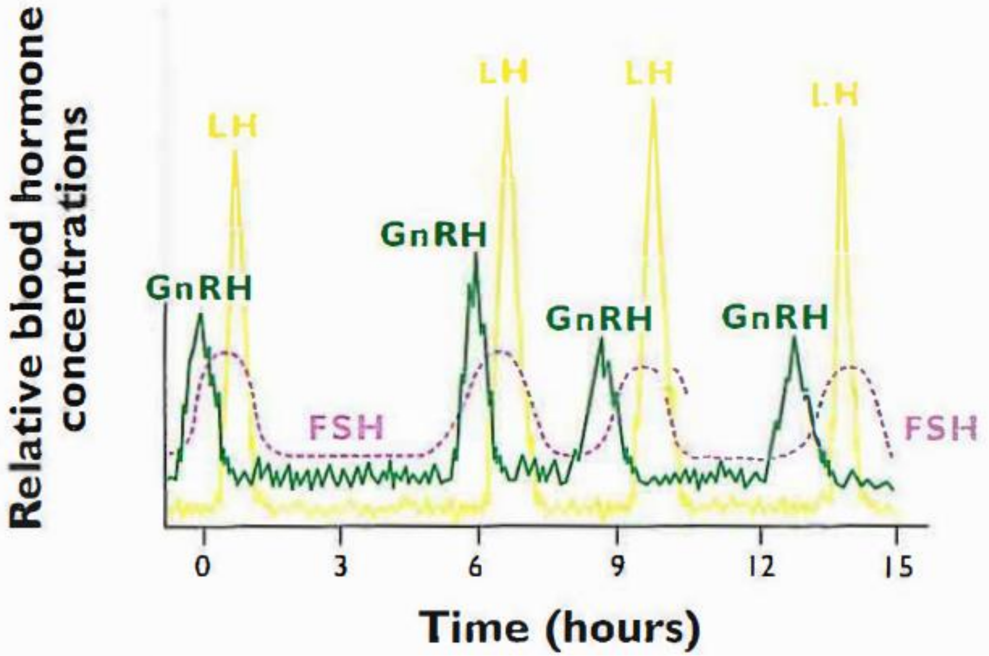
IX



After meiosis, haploid spherical spermatids differentiate into spermatozoa. Meiosis and differentiation take place in the adluminal compartment. Notice that each generation of cells is attached by intercellular cytoplasmic bridges. Thus, each generation divides synchronously in cohorts. Some cells (black) degenerate during the process. Numbers indicate the theoretical number of cells generated by each division.

Endocrine Control/Regulation of Spermatogenesis IX

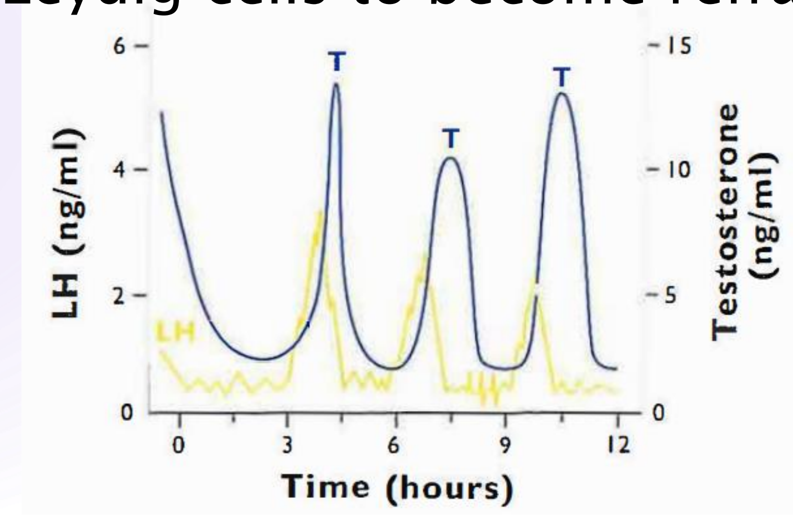
- Before spermatozoa can be produced, certain endocrine requirements must be met.
  - I) adequate secretion of GnRH from the hypothalamus;
  - 2) FSH and LH secretion from the anterior lobe of the pituitary
  - 3) secretion of gonadal steroids (testosterone and estradiol)



GnRH causes the release of LH and FSH. Episodes of all three hormones occur between 4 and 8 times in 24 hours. The lower FSH profile, when compared to LH, is due to inhibin secretion by Sertoli cells. Also, the greater duration of the FSH episode is probably due to its longer half-life (100 min) when compared to LH (30 min).

Endocrine Control/Regulation of Spermatogenesis IX

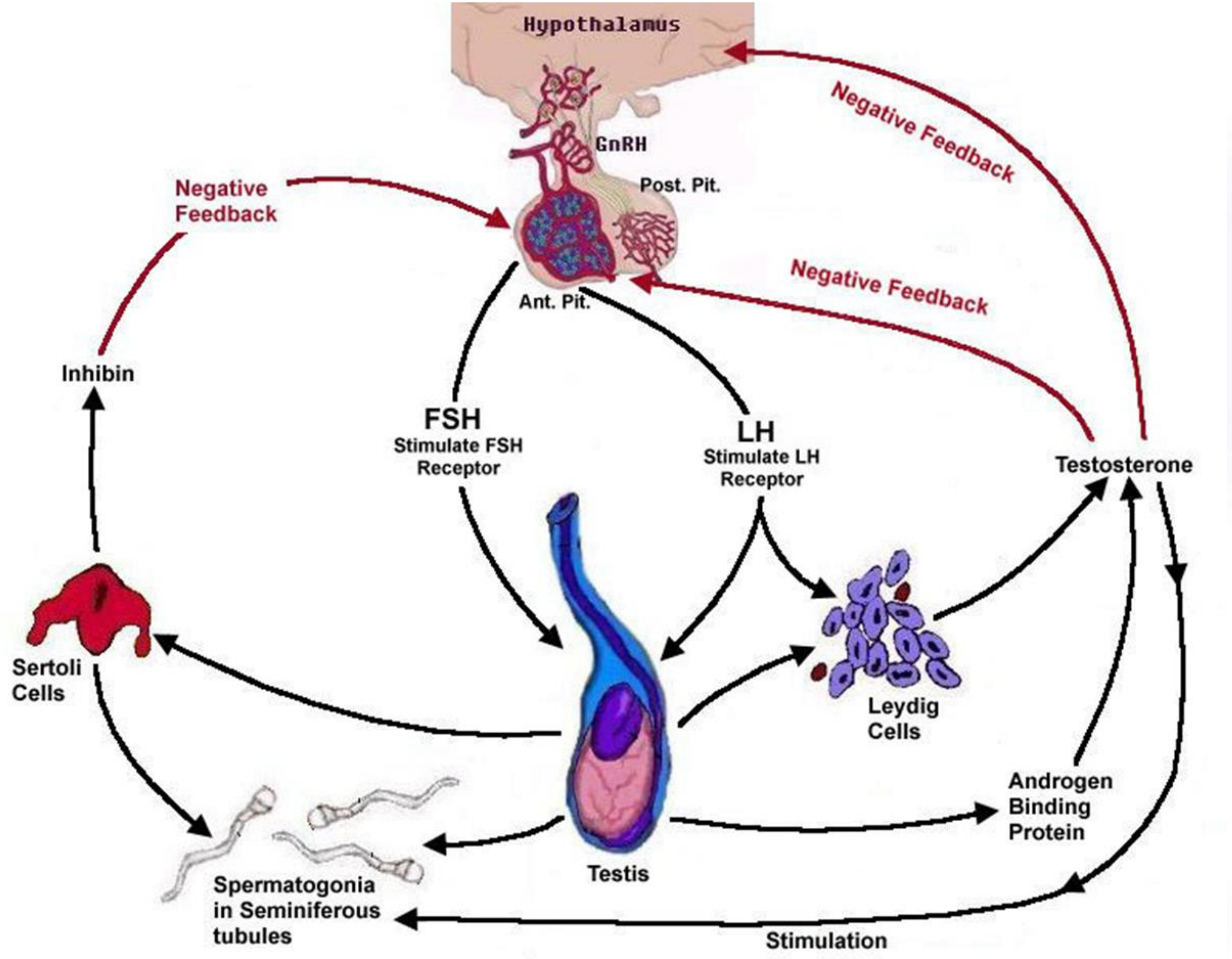
- Luteinizing hormone acts on the Leydig cells within the testes
  - Leydig cells are analogous to the cells of the theca interna of antral follicles in the ovary.
  - They contain membrane-bound receptors for LH
  - The Leydig cells synthesize and secrete testosterone less than 30 minutes after the onset of an LH episode in a pulsatile fashion.
  - Pulsatile discharge of LH is important for normal testicular function which prevents Leydig cells to become refractory (unresponsive) to LH.



LH is elevated for a period of 0.5 to 1.25 hours, while the subsequent testosterone (T) episode lasts for 0.5 to 1.5 hours.

Endocrine Control/Regulation of Spermatogenesis

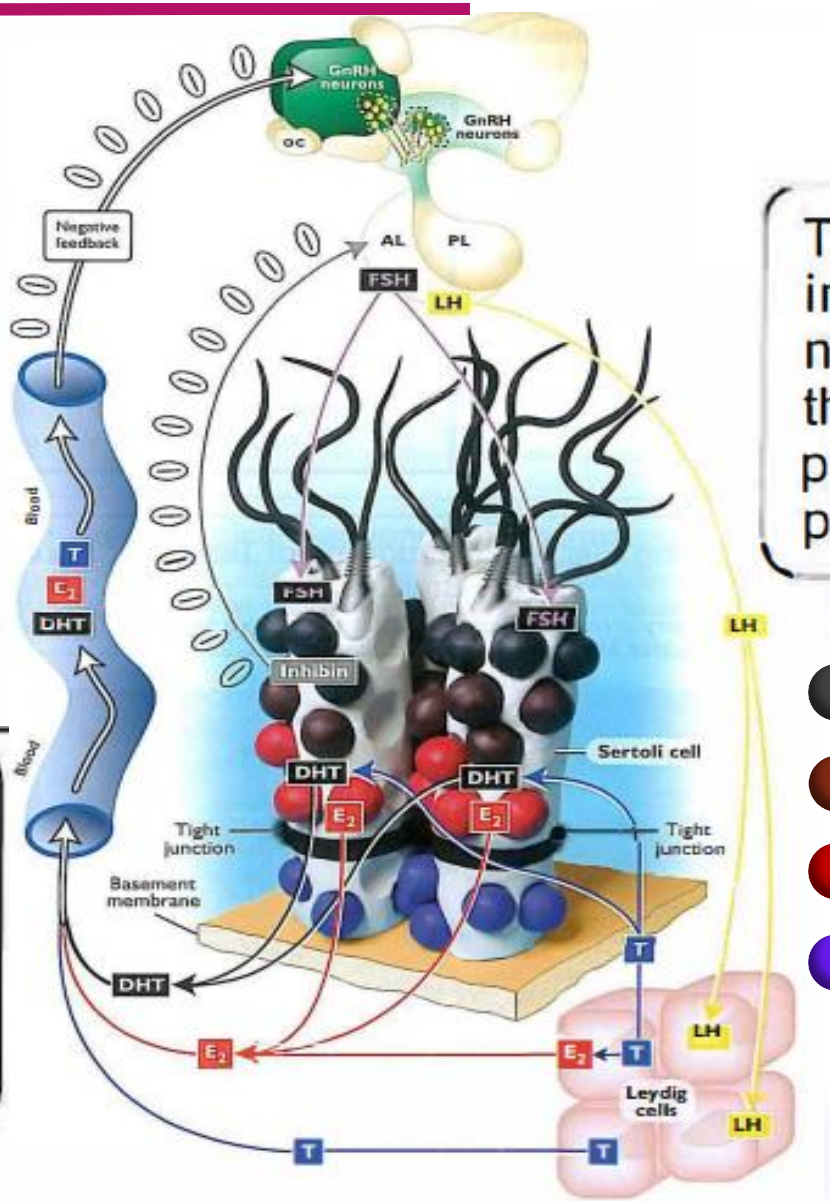
IX



Endocrine Control/Regulation of Spermatogenesis IX

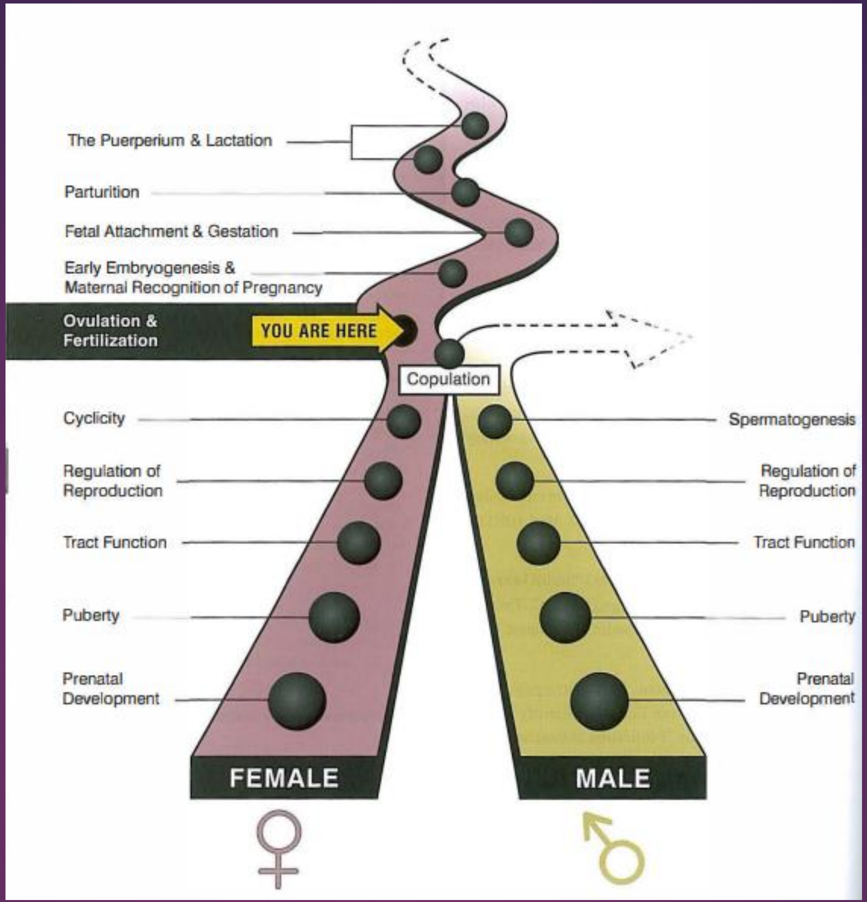
LH binds to receptors in the interstitial cells of Leydig and FSH binds to Sertoli cells. Leydig cells secrete testosterone that is transported to the adjacent vasculature and the Sertoli cells where T is converted to DHT.

Testosterone (T) secreted by the Leydig cells is transported into the Sertoli cells where it is converted to dihydrotestosterone (DHT) and also estradiol (E_2). Testosterone and E_2 are transported by the blood to the hypothalamus where they exert a negative feedback on the GnRH neurons.



The Sertoli cells secrete inhibin that exerts a negative feedback on the anterior lobe of the pituitary to directly suppress FSH secretion.

- Spermatids
- Secondary spermatocyte
- Primary spermatocyte
- Spermatogonia



Section X

Spermatozoa in the Female Tract

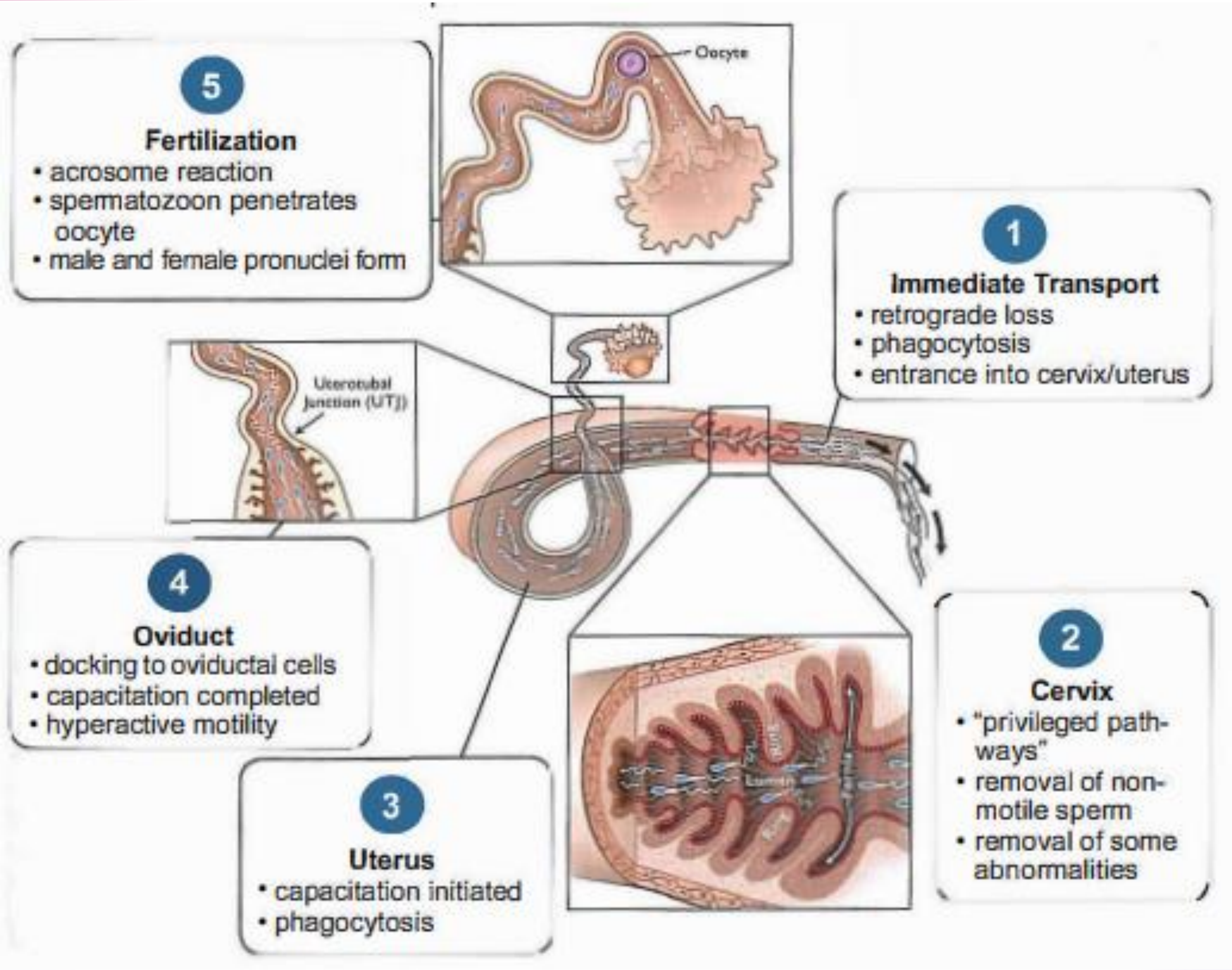
From Insemination to Fertilization

X

- Following insemination, viable spermatozoa that are retained in the female reproductive tract must:
  - 1) transverse the cervix,
  - 2) be transported through the uterus to the oviduct,
  - 3) undergo capacitation,
  - 4) bind to the oocyte,
  - 5) undergo the acrosome reaction
  - 6) penetrate the zona pellucida and fuse with the oocyte plasma membrane
- After fusion with the plasma membrane, the fertilizing spermatozoon enters the oocyte cytoplasm and its nucleus decondenses. The male pronucleus is formed. This signifies successful fertilization.

From Insemination to Fertilization

X



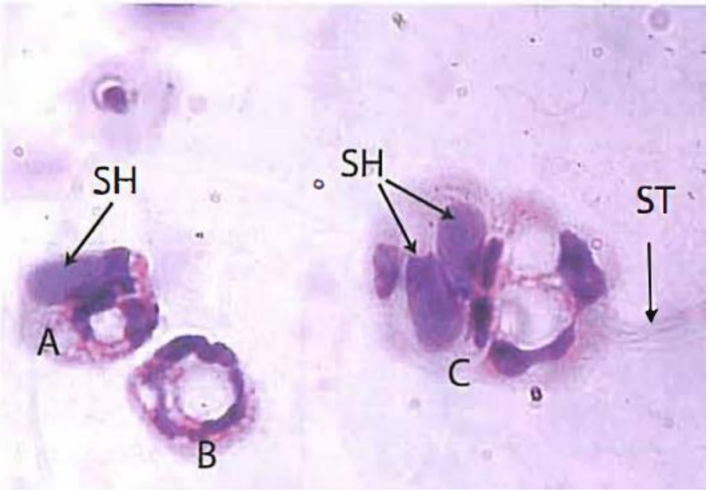
From Insemination to Fertilization

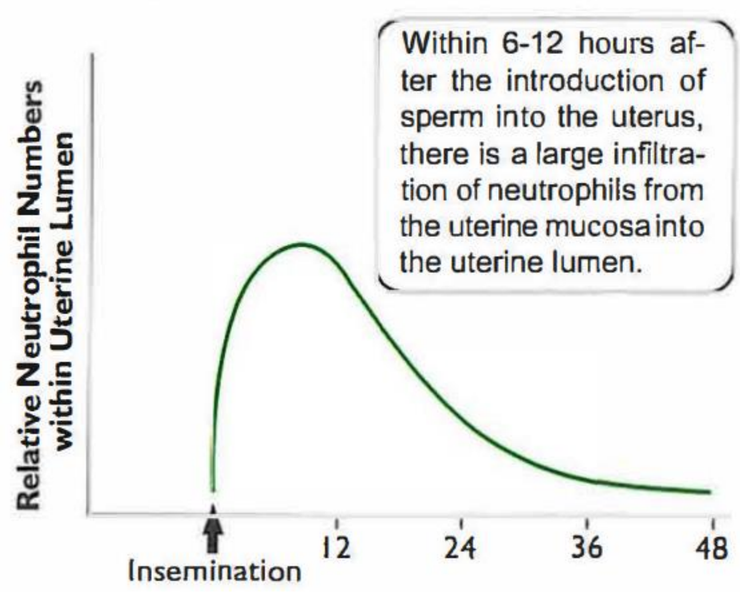
X

1. Spermatozoa are lost from the female tract by:

- phagocytosis by neutrophils
  - spermatozoa are foreign to the female, thus, neutrophils actively phagocytize spermatozoa as well as other microorganisms introduced to the female genitalia.

Three leukocytes (A,B and C) phagocytizing sperm. Sperm heads (SH) can be observed in the cytoplasm of the leukocytes. A sperm tail (ST) can also be seen protruding from the leukocyte (Micrograph courtesy of R.G. Saacke, Virginia Polytechnic Institute and State University, Blacksburg)





- retrograde transport
  - the physical nature of the ejaculate (coagulating proteins)
  - the site of seminal deposition (cranial vagina, cervix)

From Insemination to Fertilization

X

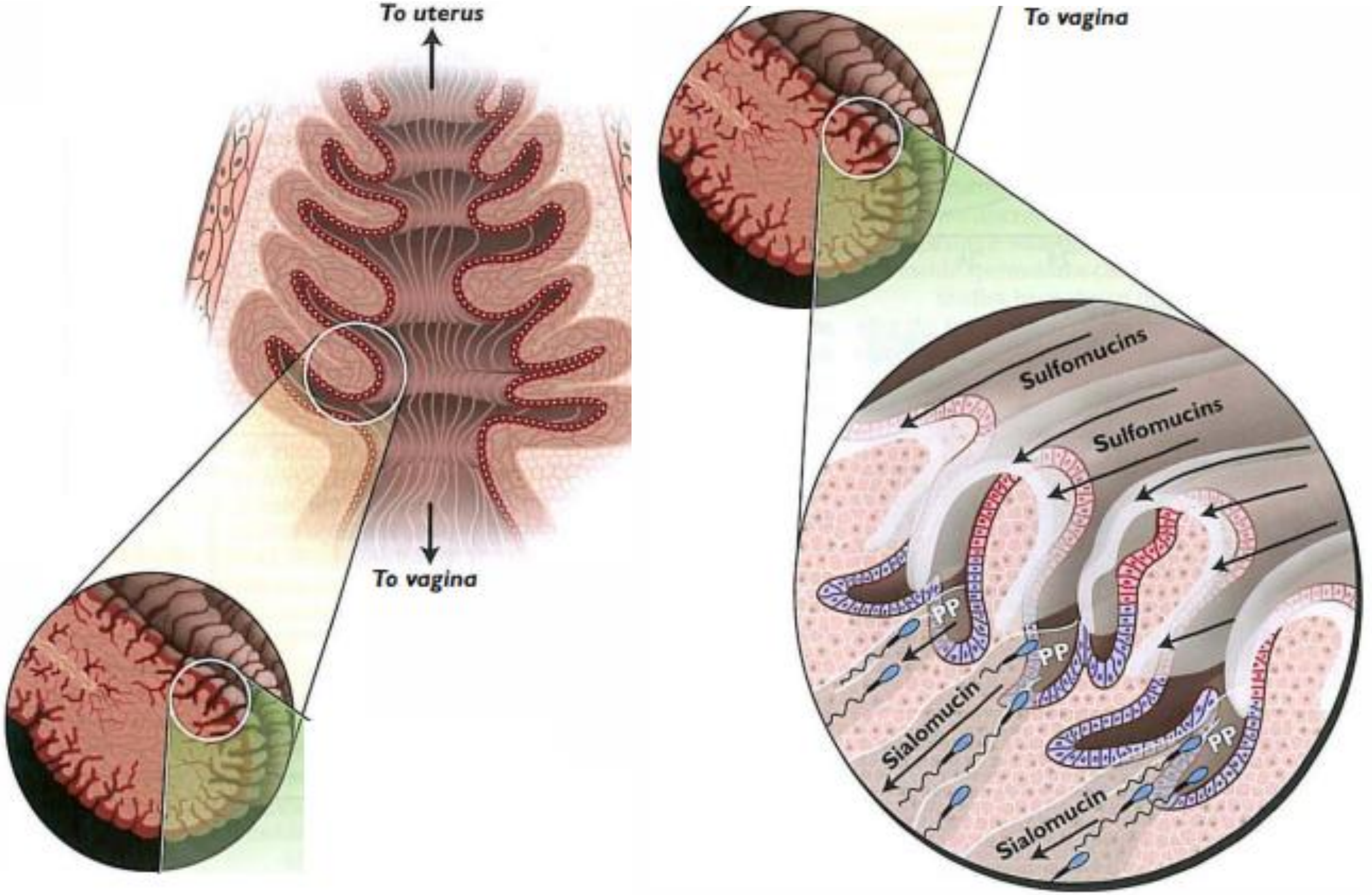
2. The cervix is a major barrier to spermatozoal transport and it can also serve as a reservoir for spermatozoa.

- During estrus, the cervix produces mucus
  - sialomucin, a mucus of low viscosity in the basal areas of the cervical crypts
  - Sulfomucin, quite viscous, produced in the apical portions of the cervical epithelium covering the tips of the cervical folds
- Spermatozoa encountering the viscous sulfomucin are washed out of the tract. Those that encounter the low viscosity sialomucin in the environment of the crypts of the cervix swim into it.
  - Thus, the low viscosity environment of the deeper cervical crypts creates "privileged pathways" through which spermatozoa can move.
  - the cervix serves as a filter that eliminates non-motile spermatozoa.

From Insemination to Fertilization

X

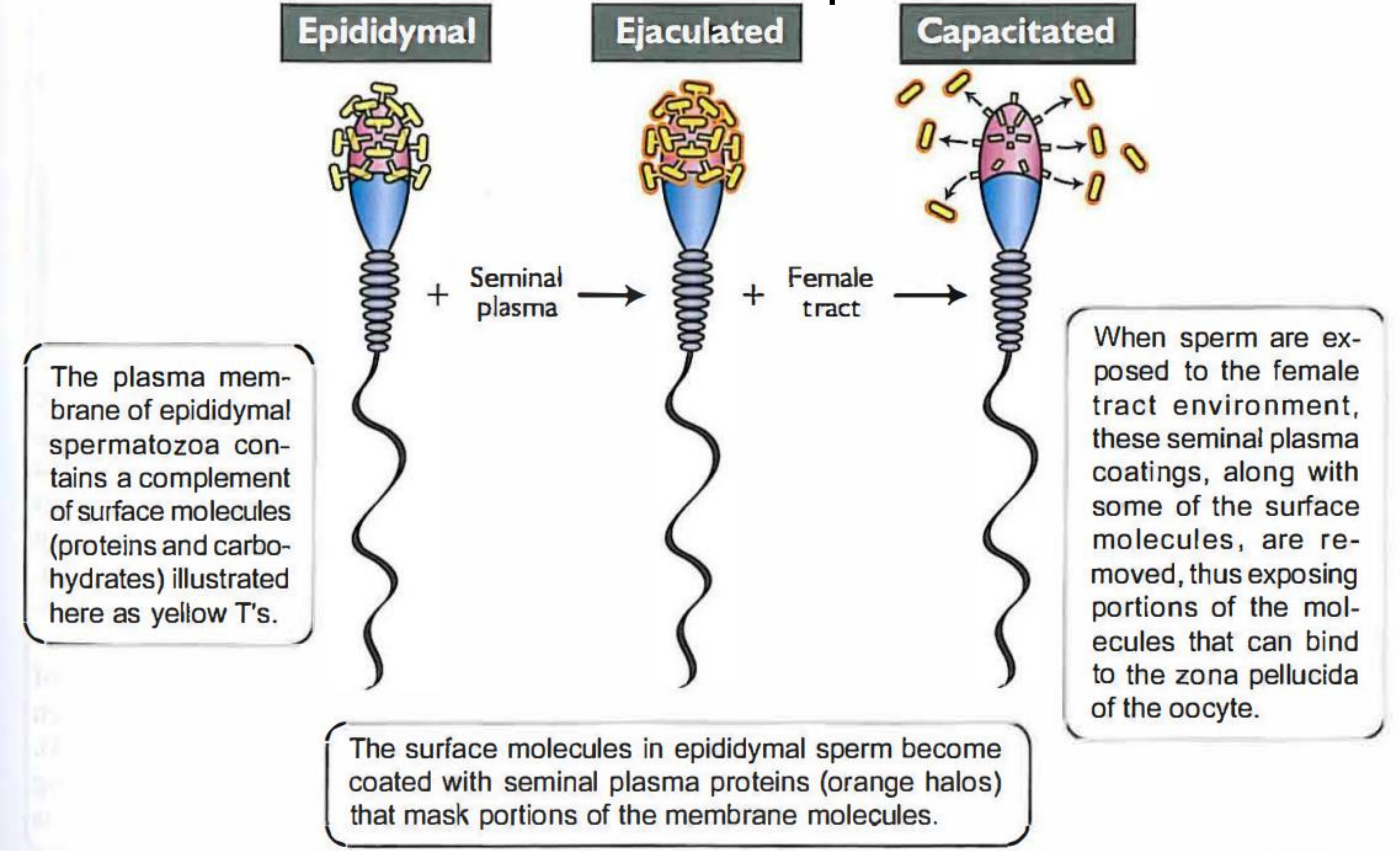
During estrus secretion of sulfomucins from the apical portion of the cervical mucosa produces sheets of viscous mucus. Secretion is toward the lumen and flows in a caudal direction. Less viscous sialomucins are produced in the basal crypts of the cervix. Spermatozoa found in the basal regions are orientated in the same direction and traverse the cervix toward the uterus through these "privileged pathways" (PP) of low viscosity sialomucin. (Modified from Mullins and Saacke 1989. *Anat. Rec.* 225:106)



From Insemination to Fertilization

X

3. Capacitation is a process that refers to the changes that allow the spermatozoa to become fertile. This process is reversible!



From Insemination to Fertilization

X

4. Hyperactive motility occurs in the oviduct.

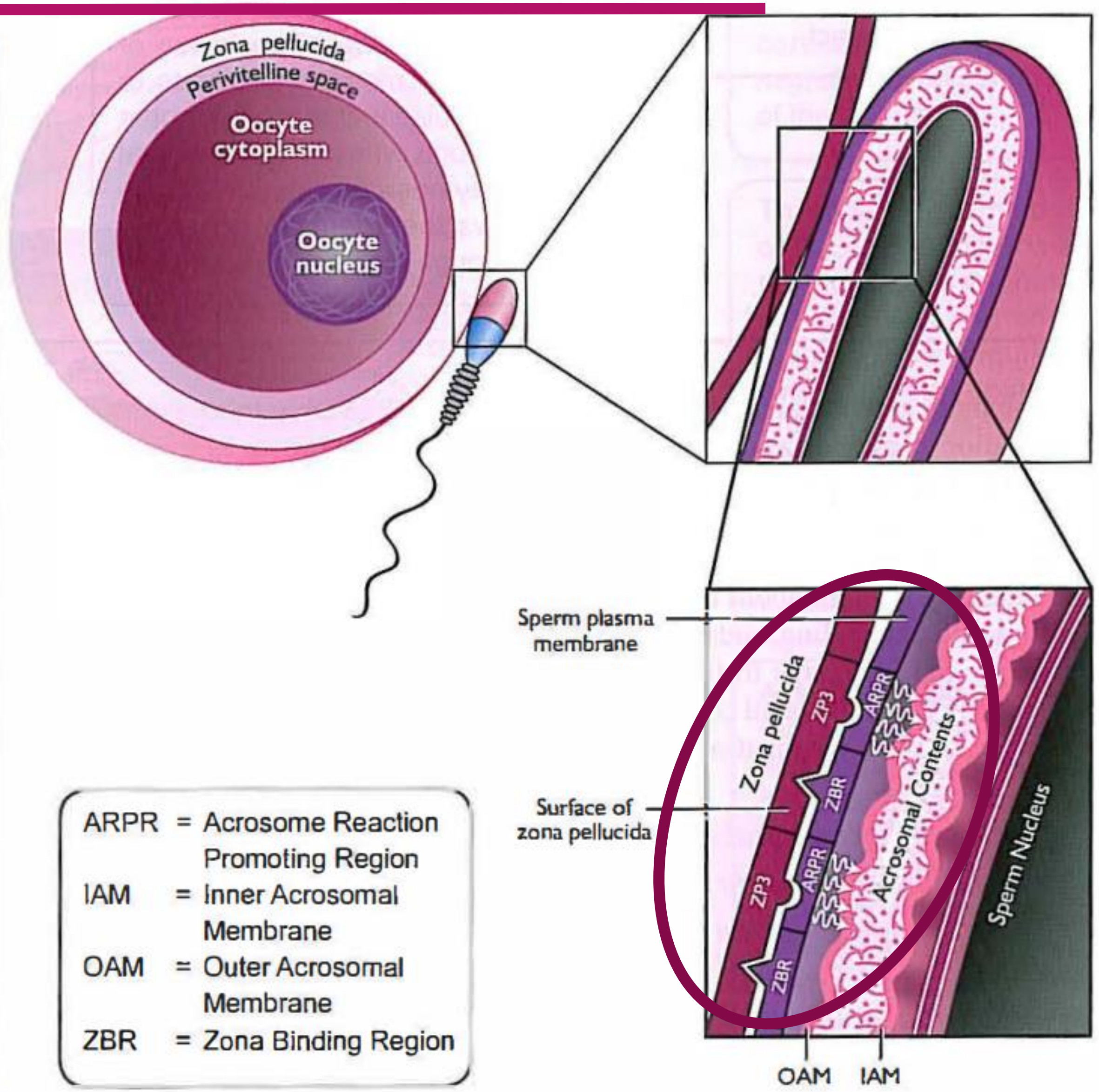
- The spermatozoal motility pattern changes from a progressive, linear motility into a dancing motion that is not linear and is localized in a small area which facilitates sperm-oocyte contact.

5. Binding of spermatozoa and zona pellucida requires specific proteins of both sides for attachment.
   - Female side: Zona proteins 1, 2 and 3 (ZP1, ZP2 and ZP3)
     - ZP1 & ZP2 are structural
     - ZP3 attaches to the spermatozoon (10,000 to 50,000 required)
   - Male side: Primary zona binding region (ZBR): adheres to the ZP3 of the zona pellucida
   - Acrosome reaction promoting ligand (ARPR): binds with ZP3 and starts a signal transduction which initiates the acrosomal reaction

From Insemination to Fertilization

X

Proposed model for zona binding and the initiation of the acrosomal reaction in mammalian spermatozoa. The sperm plasma membrane overlying the acrosome contains two receptor-like regions. The first, called the zona binding region (ZBR), reacts with ZP3 to cause physical attachment of the sperm to the zona pellucida. A second membrane region, the acrosome reaction promoting region (ARPR), also binds to ZP3 and initiates the acrosome reaction by causing the sperm plasma membrane to fuse (arrows) to the outer acrosomal membrane.



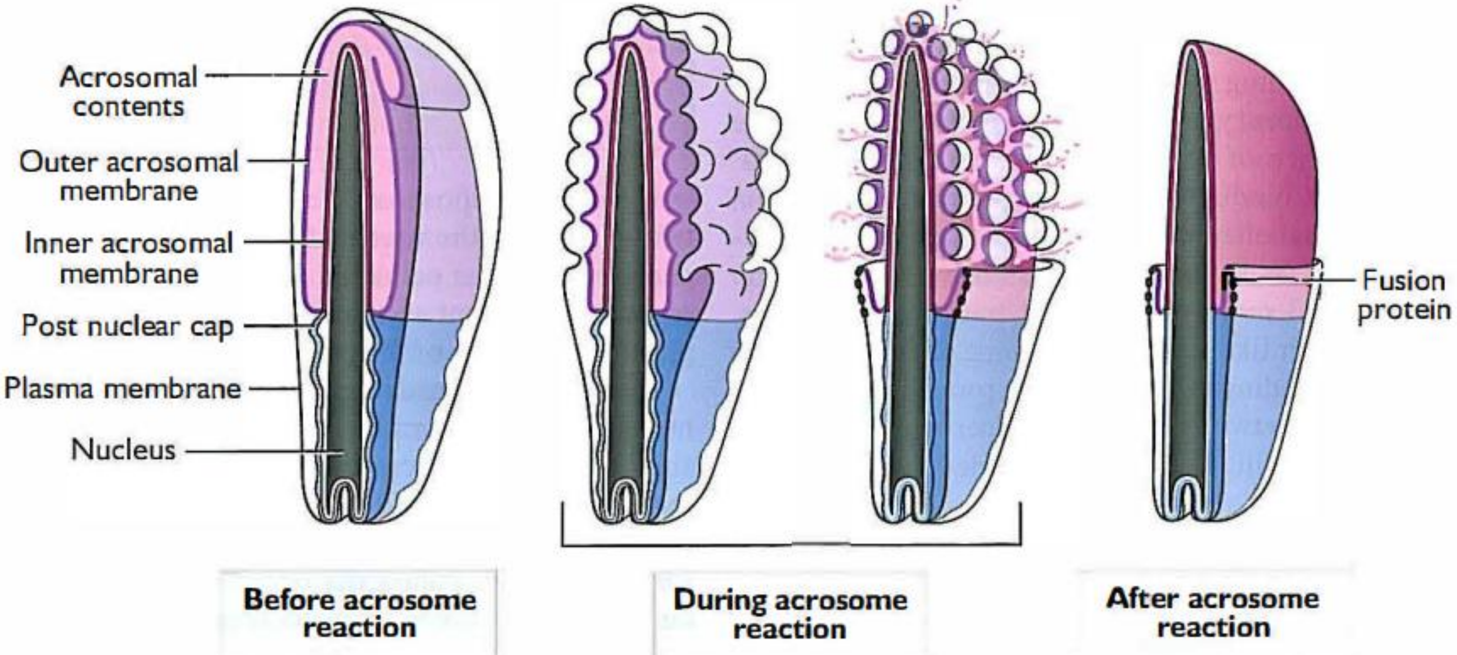
From Insemination to Fertilization

X

6. Acrosomal Reaction: The purpose of the acrosomal reaction is:
   - First, the reaction enables spermatozoa to penetrate the zona pellucida.
   - Second, it modifies the equatorial segment so that it can later fuse with the plasma membrane of the oocyte.

- The acrosomal reaction begins when the plasma membrane of the spermatozoon forms multiple fusion sites with the outer acrosomal membrane.
- When the two membranes fuse, many small vesicles are formed and this process is called vesiculation. After vesiculation has occurred, the sperm nucleus is left with the inner acrosomal membrane surrounding it.
- Following attachment to the zona pellucida, the acrosome reaction allows the release of a variety of enzymes
  - Acrosin: hydrolyzes zona proteins and enhances the sperm's bind to the zona.
  - Fusion protein: fuses the oocyte plasma membrane with the equatorial segment of the spermatozoa

From Insemination to Fertilization



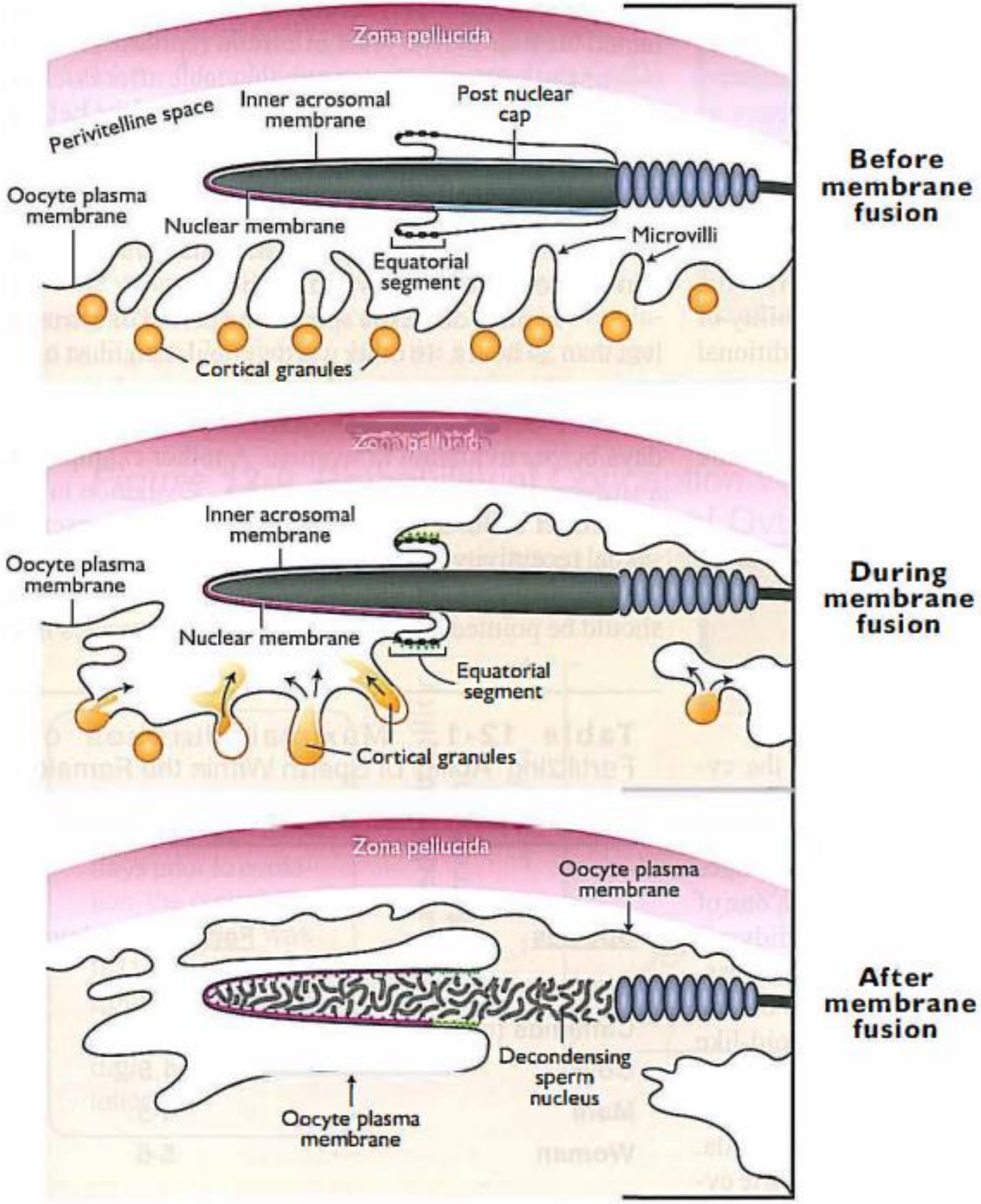
Before Acrosomal Reaction
Before the reaction begins, all membranes of the head are intact.

During Acrosomal Reaction
During the reaction, the plasma membrane overlying the acrosomal membrane begins to fuse with the outer acrosomal membrane. The fusion of the two membranes leads to vesiculation that creates pores through which the acrosomal enzymes can pass. This allows the sperm to penetrate through the zona pellucida.

After Acrosomal Reaction
After the reaction, the vesicles are sloughed, leaving the inner acrosomal membrane, the equatorial segment and the post nuclear cap intact.

Fertilization

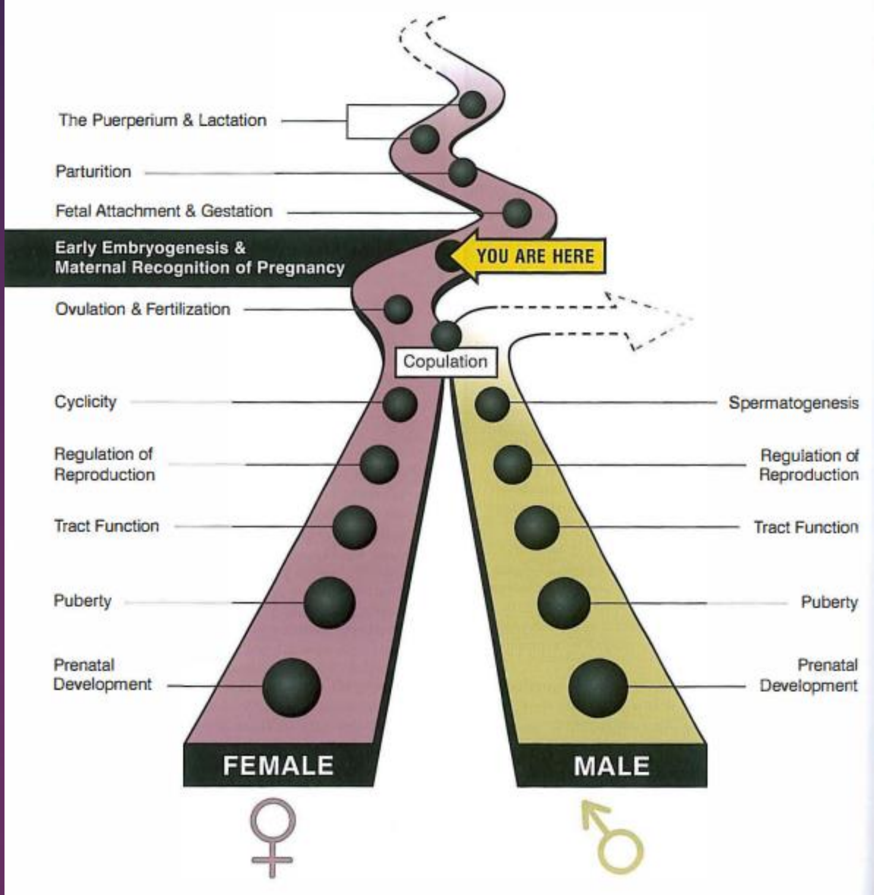
- the acrosomal reaction allows the spermatozoon to digest a small hole through the zona through which it can pass.
- After membrane fusion, cortical reaction happens
- Exocytosis of the cortical granules results in the zona block, a process whereby the zona pellucida undergoes biochemical changes so that further sperm cannot penetrate it.



When the spermatozoon completely penetrates the zona and reaches the perivitelline space, it settles into a bed of microvilli formed by the oocyte plasma membrane. The cortical granules have migrated to the periphery of the oocyte.

The plasma membrane of the oocyte fuses with the equatorial segment and the fertilizing spermatozoon is engulfed. The cortical granule membrane fuses with the oocyte plasma membrane and the cortical contents are released into to perivitelline space by exocytosis.

After the fusion between the membrane of the equatorial segment and the oocyte plasma membrane occurs, the nucleus of the spermatozoon is within the cytoplasm. The sperm nuclear membrane disappears and the nucleus of the sperm decondenses.



Section XI

Early Embryogenesis

& Maternal Recognition of Pregnancy

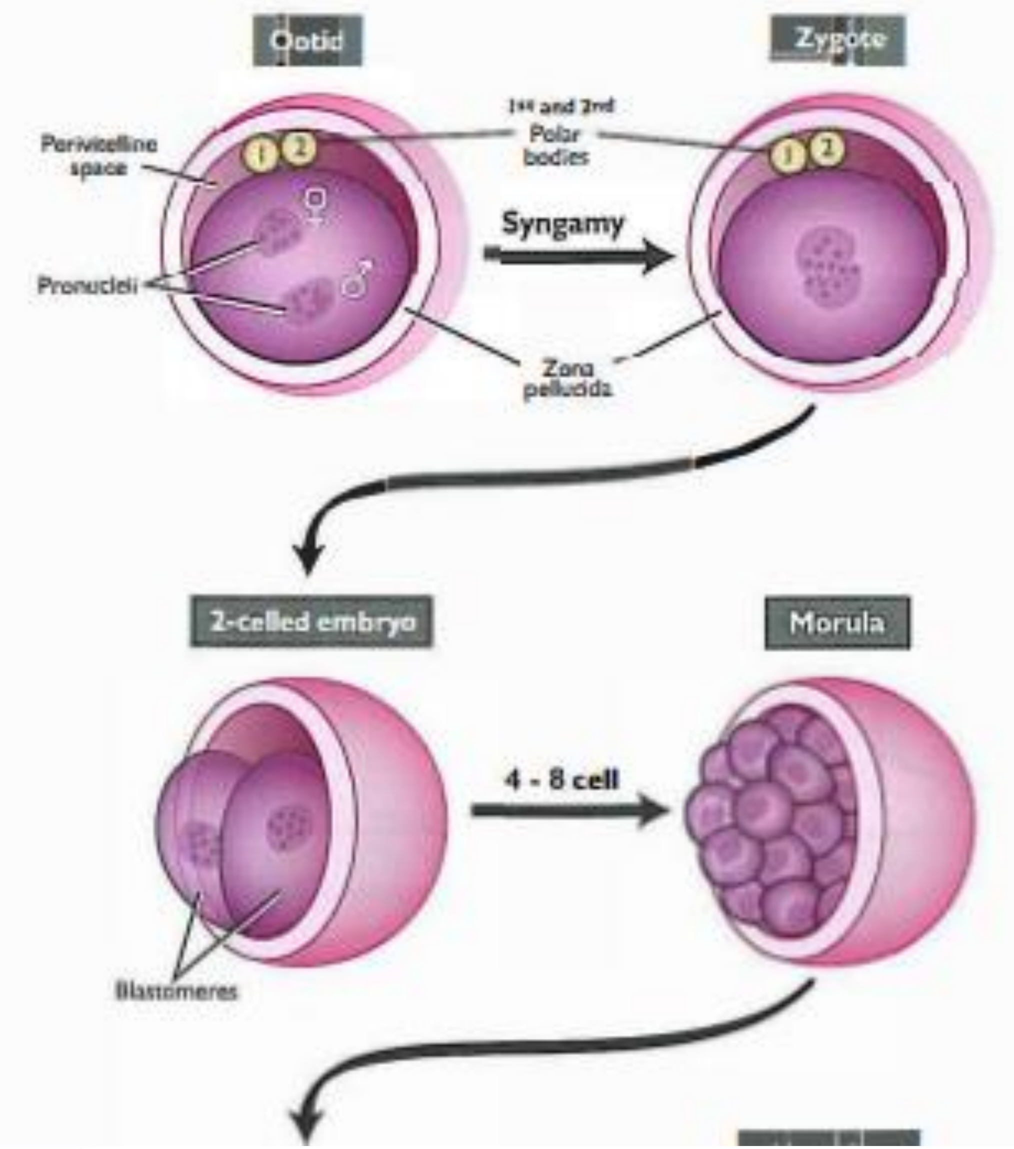
Embryological Terminology

XI

- Syngamy: fusion of the male and female pronuclei
- Zygote: a 2n chromosomal cell formed by sperm and ova fertilization
- Embryo: an organism in the early stages of development.
  - an embryo has not acquired an anatomical form that is readily recognizable in appearance as a member of the specific species.
- Fetus: a potential offspring that is still within the uterus, but is generally recognizable as a member of a given species.
- Conceptus: is the product of conception. It includes:
  - 1) the embryo during the early embryonic stage,
  - 2) the embryo and extraembryonic membranes during the preimplantation stage,
  - 3) the fetus and placenta during the post-attachment phase.

Preattachment Development of the Embryo

XI

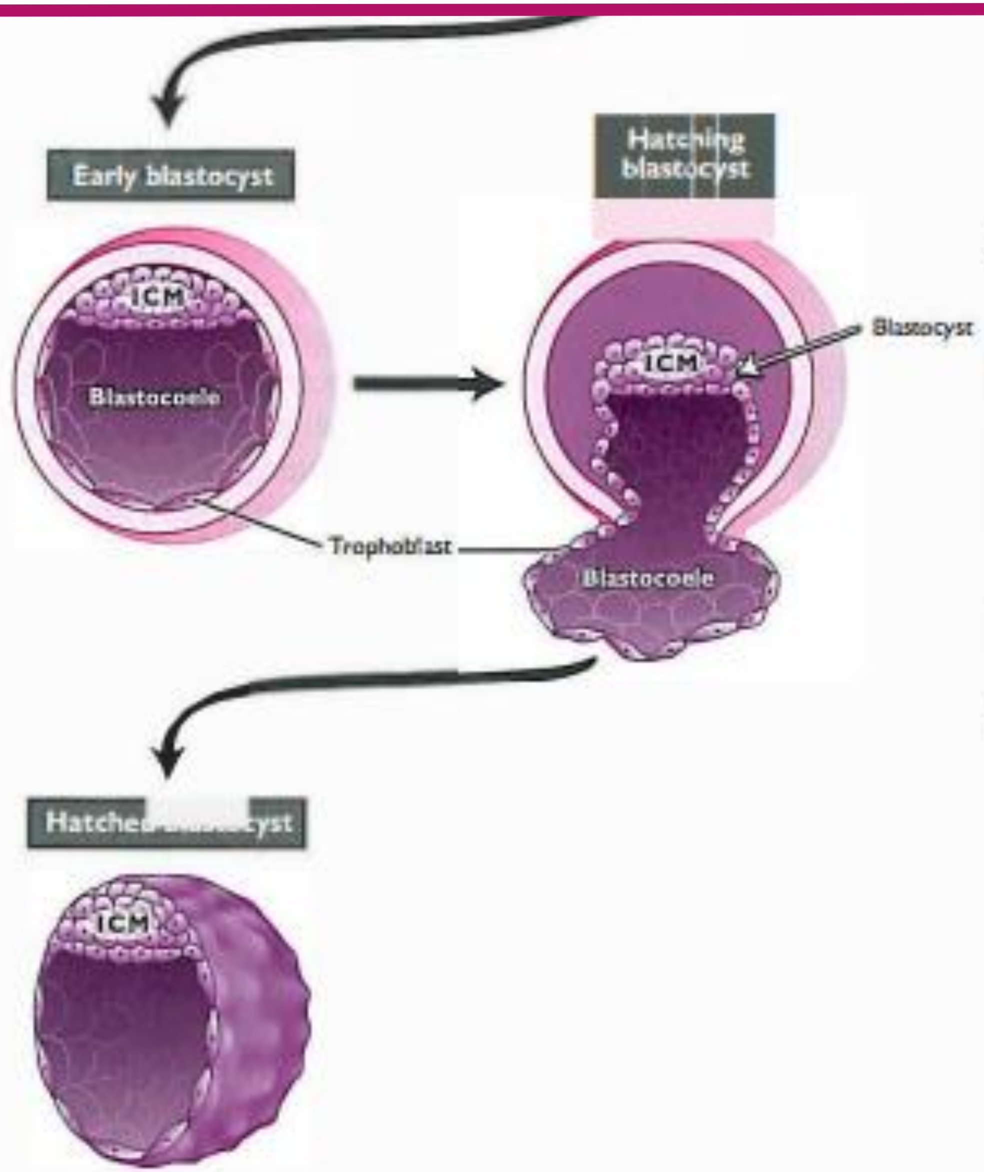


In the ootid, male and female pronuclei along with the first and second polar bodies are present. Fusion of the male and female pronuclei into a single diploid nucleus constitutes syngamy. Shortly thereafter, the zygote undergoes cleavage (mitotic divisions) and gives rise to daughter cells called blastomeres.

Cleavage divisions continue. A four-celled embryo gives rise to an eight-celled embryo. After the eight-celled stage, a ball of cells is formed and this embryonic stage is referred to as a morula.

Preattachment Development of the Embryo

XI

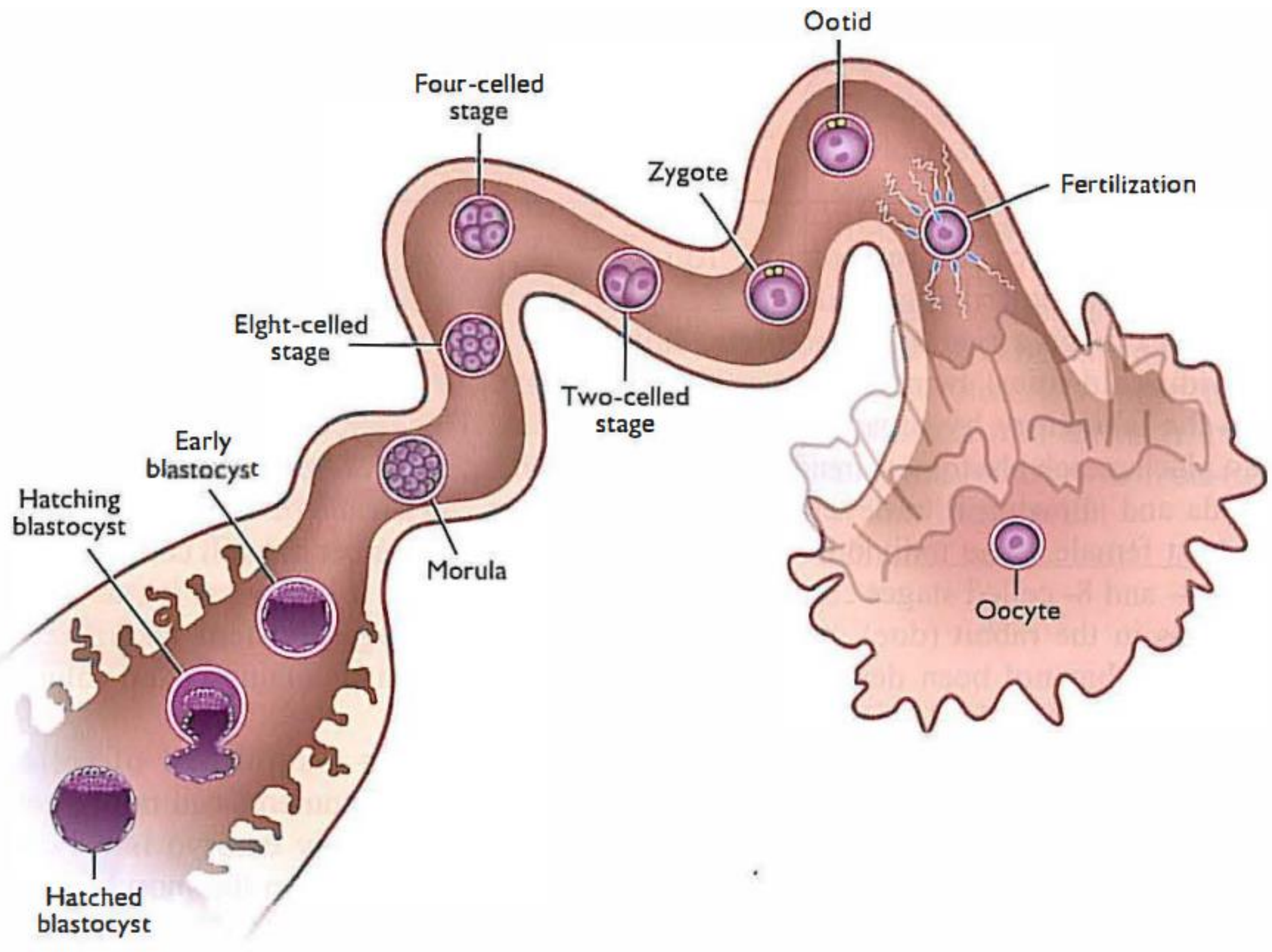


Cells of the morula continue to divide and a blastocyst develops. It consists of an inner cell mass (ICM), a cavity called the blastocoele and a single layer of cells called the trophoblast. Finally, the rapidly growing blastocyst "hatches" from the zona pellucida and forms a "hatched" blastocyst that is free-floating within the uterus.

Preattachment Development of the Embryo

XI

- The inner cell mass will give rise to the body of the embryo.
- The trophoblastic cells will eventually give rise to the chorion.
- The chorion will become the fetal component of the placenta



Development of Extraembryonic Membranes

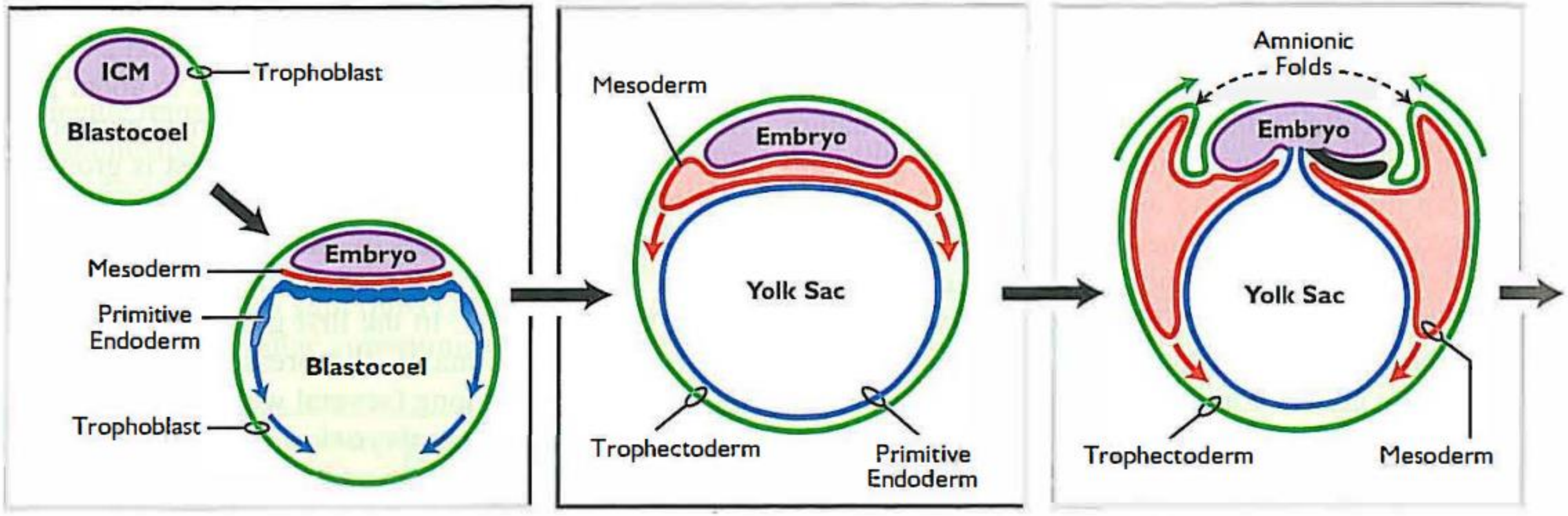
XI

(This developmental sequence must occur before attachment to the endometrium can take place)

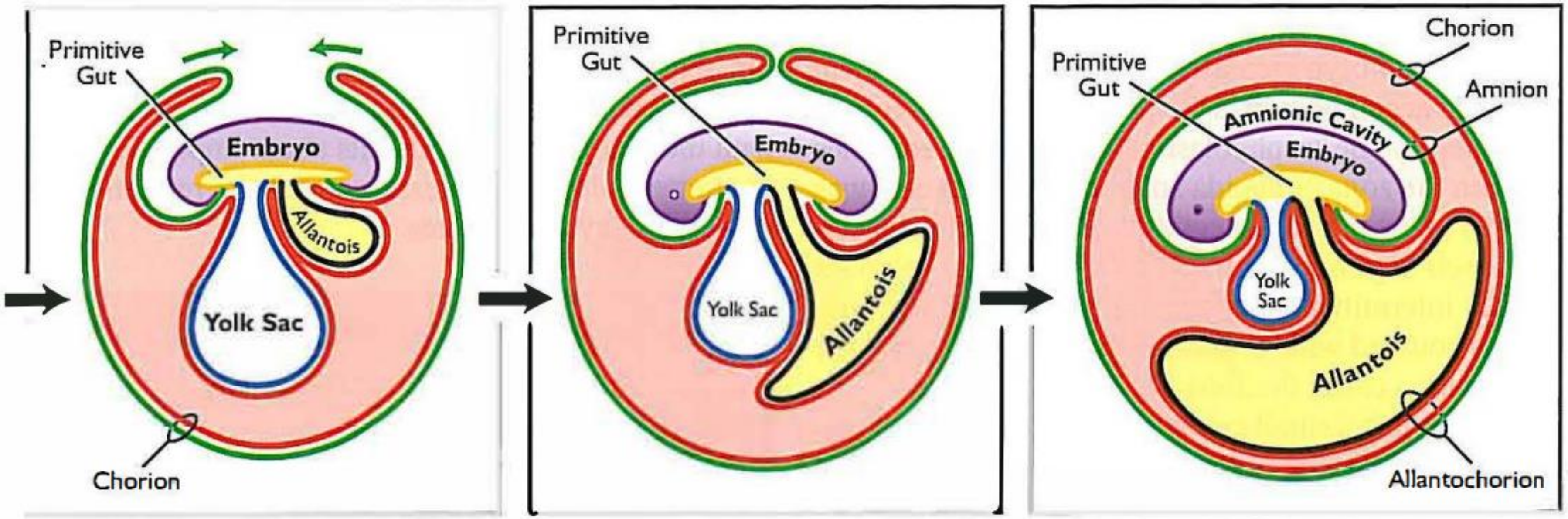
The hatched blastocyst consists of the inner cell mass (ICM), the trophoblast and the blastocoele. Very early in embryonic development, the primitive endoderm (blue layer) begins to form beneath the inner cell mass and grows downward forming a lining on the inner surface of the trophoblast. At the same time, the mesoderm (red layer) begins to develop between the primitive endoderm and the embryo.

When the primitive endoderm completes its growth, it forms a cavity called a yolk sac. This cavity does not contain yolk but is so named because it is analogous to the yolk sac in avian embryos.

The mesoderm continues to grow, forming a sac that surrounds the yolk sac and pushes against the trophectoderm (previously the trophoblastic cells). The newly formed mesodermal sac pushes against the trophectoderm and begins to fold upward forming "wing-like" structures called amnionic folds.



Development of Extraembryonic Membranes



The mesoderm now completely surrounds the yolk sac and the developing allantois. The allantois is a diverticulum from the primitive gut that collects embryonic wastes. The mesoderm continues to fuse with the cells of the trophectoderm to form the chorion. The amnionic folds continue to grow upward around the embryo.

The yolk sac begins to regress but the allantois continues to grow and expand. The amnionic folds almost completely surround the embryo. The leading edges of the amnionic folds will eventually fuse.

The amnionic folds have completely fused resulting in the formation of a double sac around the embryo. The inner sac consists of trophectoderm and mesoderm and is called the amnion. It creates the amnionic cavity. The chorion completely surrounds the entire conceptus. The allantois continues to expand and begins to fill-in the spaces of the cavity. Eventually, the allantois and the chorion will fuse forming the allantochorion. The yolk sac continues to regress.

Maternal Recognition of Pregnancy.

XI

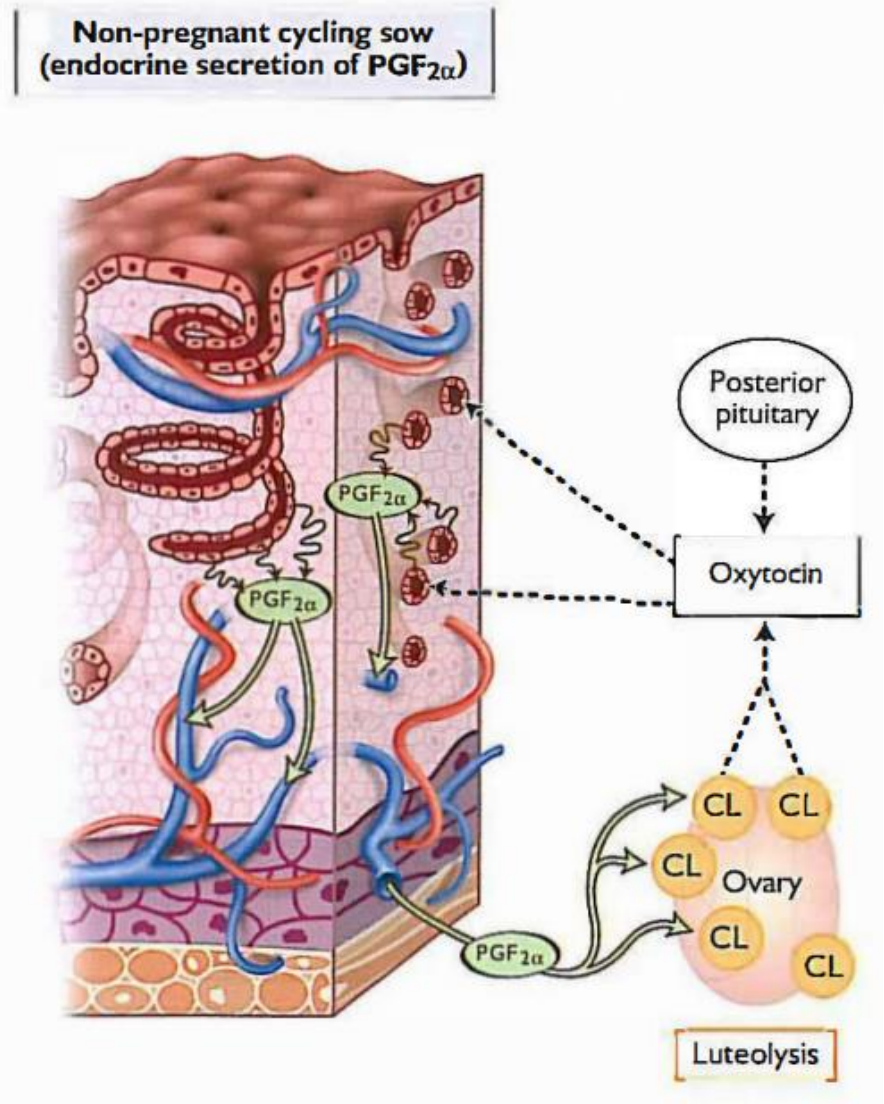
- For developing early embryogenesis to an established pregnancy:
  - luteolysis must be prevented.
  - Progesterone must be maintained at sufficiently high levels so that embryogenesis and attachment of the developing conceptus to the endometrium can take place.
- If an adequate signal is not delivered in a timely manner, the dam will experience luteolysis, progesterone concentrations will decline and pregnancy will be terminated.

Species	Pregnancy Recognition Factors	Critical Period for Recognition (days after ovulation)	Time of Attachment (days after ovulation)
Bitch	none needed	—	—
Cow	bIFN-τ (bTP-1)	15-16	18-22
Ewe	oIFN-τ (oTP-1)	13-14	15-18
Mare	3 Proteins/Estrogens = ?	12-14	36-38
Queen	none needed	—	—
Sow	Estradiol (E_2)	11-12	14-18
Woman	hCG	7-12	9-12

Maternal Recognition of Pregnancy.

XI

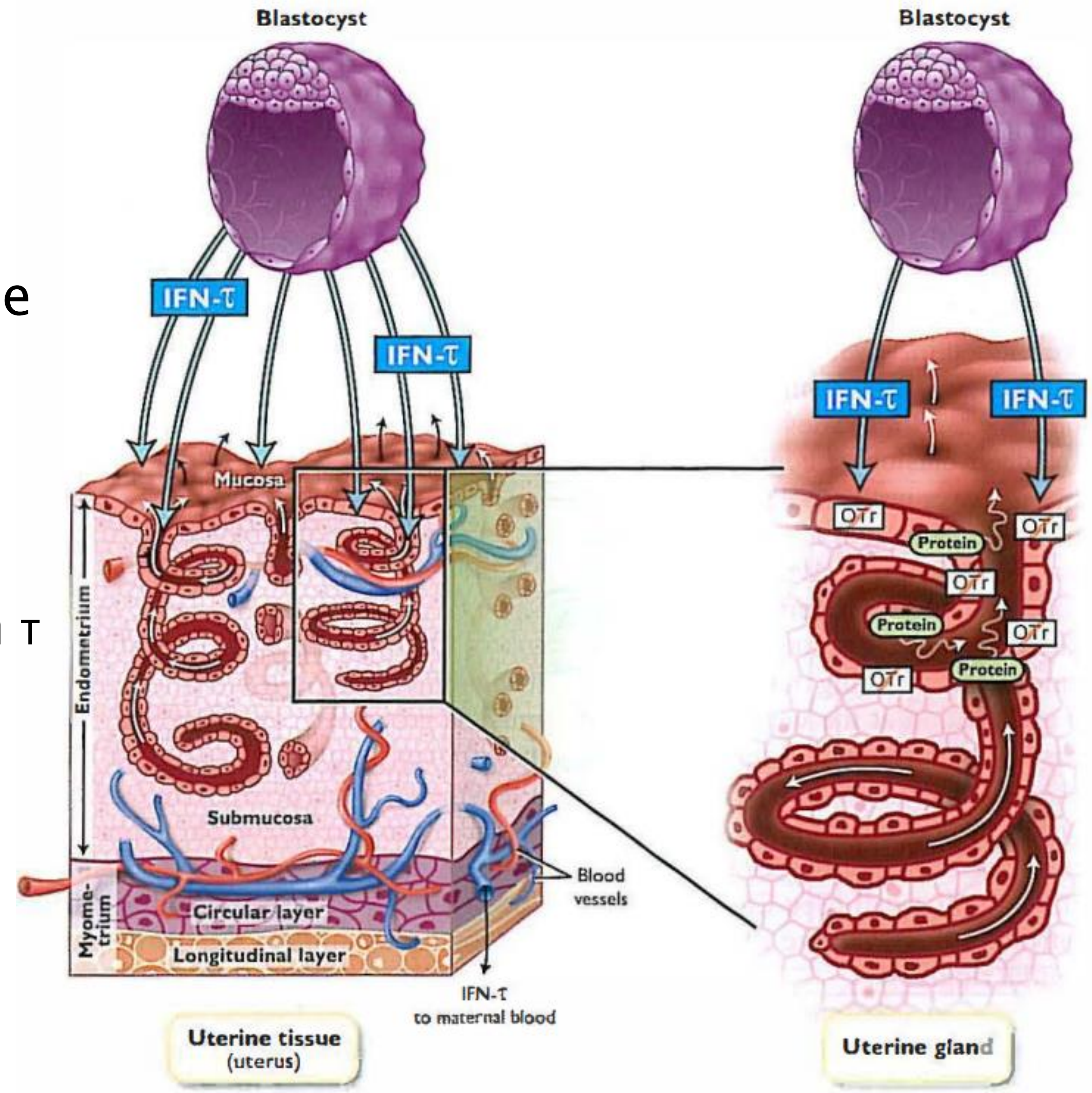
- the corpus luteum of ruminants produces oxytocin that stimulates endometrial cells to synthesize $PGF_{2\alpha}$.
- The production of $PGF_{2\alpha}$ is dependent upon a threshold number of oxytocin receptors that are synthesized by endometrial cells at a critical time during the estrous cycle.
- When these receptors are available in sufficient numbers, pulsatile secretion of $PGF_{2\alpha}$ occurs in response to luteal oxytocin secretion and luteolysis follows.
- Clearly, this mechanism must be prevented if a successful pregnancy is to proceed.



Maternal Recognition of Pregnancy.

XI

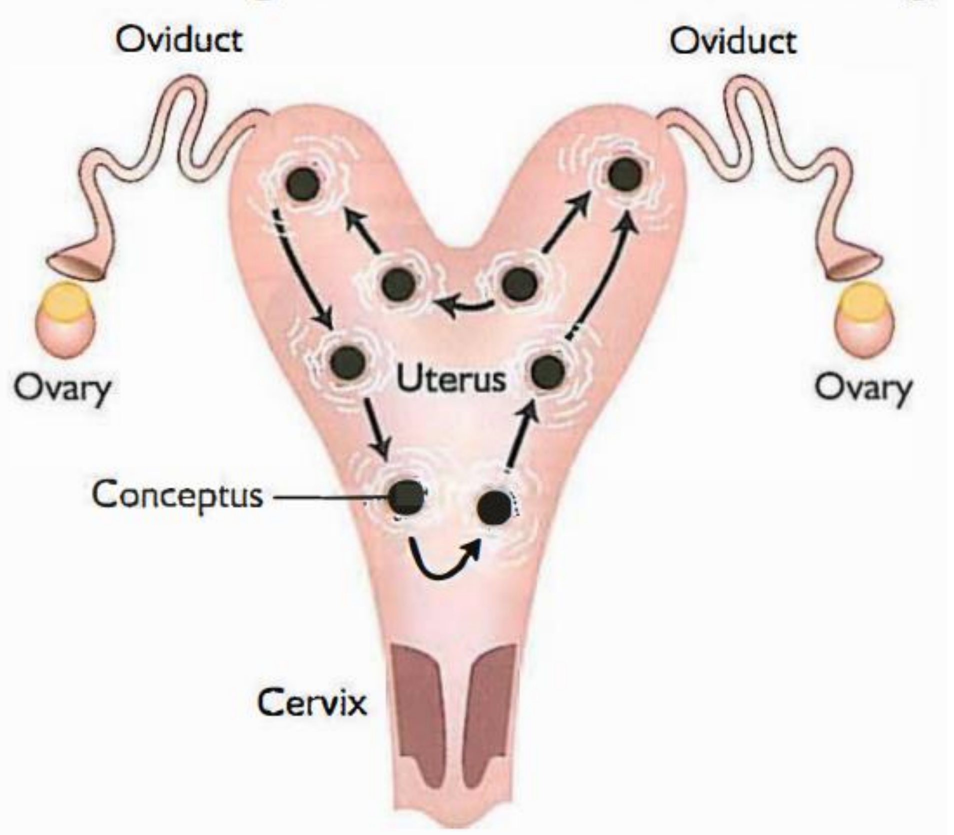
- In the ewe and the cow the free-floating blastocyst produces specific proteins that provide the signal for prevention of luteolysis.
- The specific proteins were once called ovine trophoblastic protein 1(oTP-1) and bovine trophoblastic protein 1 (bTP-1).
  - Both of these proteins belong to a class of materials known as interferons.
  - They are now referred to as ovine Interferon τ (oIFN- τ) and bovine Interferon τ (bIFN- τ).
- Secretion of progesterone by the corpus luteum is not be enhanced by oIFN- τ and therefore it is not luteotrophic. Instead, oIFN- τ binds to the endometrium and inhibits oxytocin receptor synthesis by endometrial cells



Maternal Recognition of Pregnancy.

XI

- In the mare, the presence of the conceptus prevents luteolysis.
- A unique feature of maternal recognition of pregnancy in the mare is that the conceptus is translocated over the endometrial surface by uterine contractions. The conceptus is moved from one uterine horn to the other.
  - This movement must occur between 12 and 14 times per day during days 12, 13 and 14 of pregnancy in order to inhibit $PGF_{2\alpha}$.
  - The intrauterine movement of the equine conceptus appears necessary because the conceptus does not elongate as in other species. Therefore, there is less contact between the conceptus and the endometrial surface.



Each black sphere represents a "stopping spot" in which the conceptus will spend between 5 and 20 minutes. The migration of the conceptus probably distributes pregnancy factors (white lines) over a wide surface of the endometrium.

Maternal Recognition of Pregnancy.

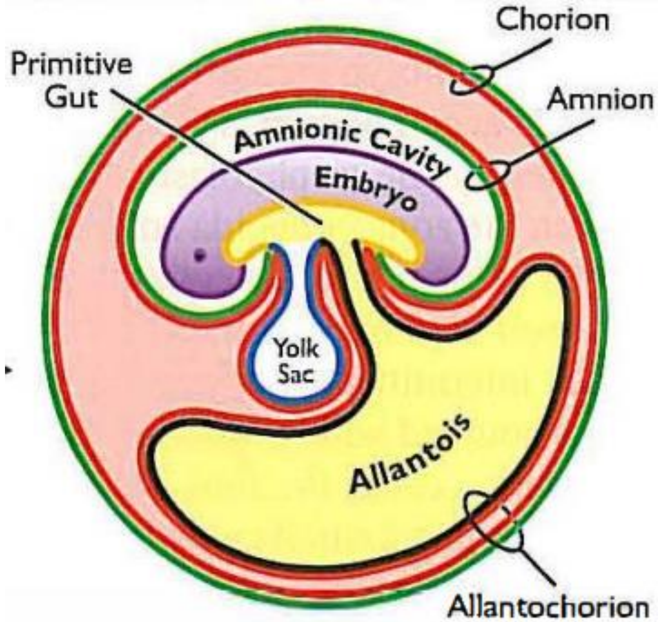
XI

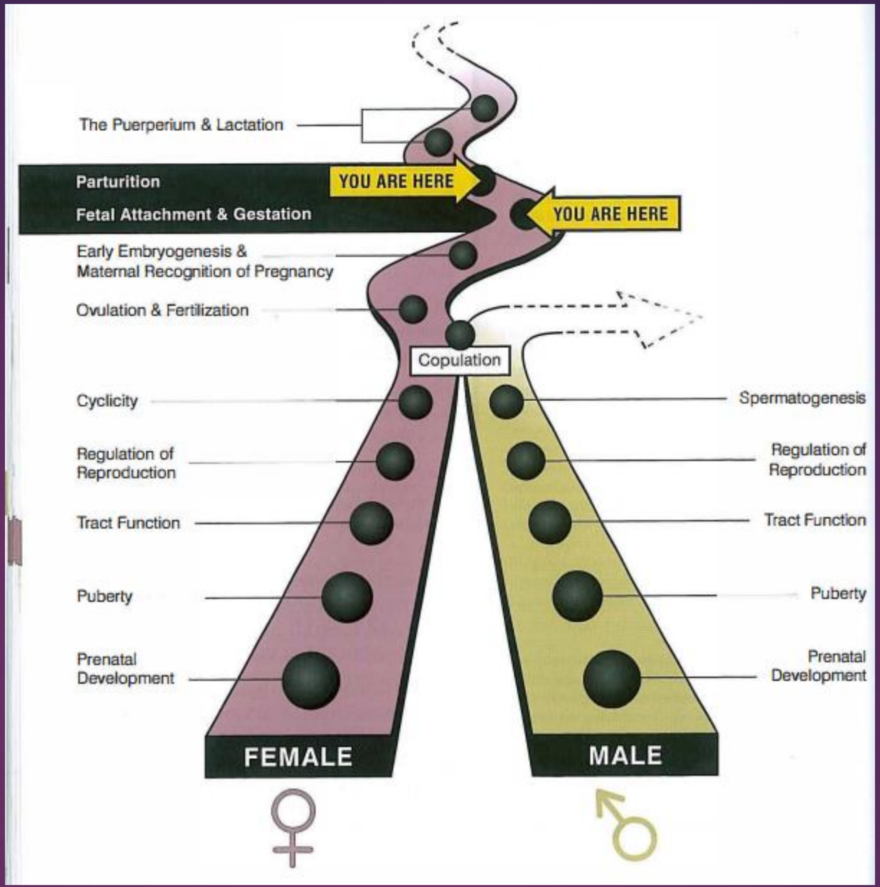
- At about the time of implantation (day 7-9 after ovulation) the human conceptus begins to secrete a hormone called human chorionic gonadotropin (hCG).
  - This is an LH-like hormone that acts on the corpus luteum to inhibit intraovarian luteolysis.
  - The precise mechanism whereby hCG blocks luteolysis is not known. Regardless, the luteotrophic effect of hCG is sufficient to allow for implantation and maintenance of pregnancy.
- In the bitch, the CL of pregnancy and the CL of the cycle have similar lifespans. Therefore, under normal cyclic conditions, the CL is long-lived
- In the queen that has been bred, a CL forms and the duration is the same as gestation (about 60 days).
  - Like the bitch, a signal from the conceptus is not needed because corpora lutea are not lysed before a pregnancy is established.

Maternal Recognition of Pregnancy.

XI

- Regardless of whether or not specific pregnancy recognition signals are provided, progesterone concentrations in the blood of the dam must be maintained at sufficiently high concentrations so that the conceptus will grow and develop.
- The extraembryonic membranes will form an attachment with the endometrium to provide a semipermanent link between the dam and the fetus.
  - This semipermanent link is known as the placenta





Section XII

Placentation

The Placenta

XII

- The final prepartum steps of reproduction are:
  - formation of a placenta
  - acquisition of endocrine function of the placenta
  - initiation of parturition
- The placenta is an organ of metabolic interchange between the conceptus and the dam. It is also an endocrine organ.
- The placenta is composed of a fetal component derived from the chorion and a maternal component derived from modifications of the uterine endometrium.
  - The discrete regions of contact between the chorion and the endometrium form specific zones of metabolic exchange.
  - The endocrine function of the placenta is important for the maintenance of pregnancy and the induction of parturition.

Maternal-Fetal Connection

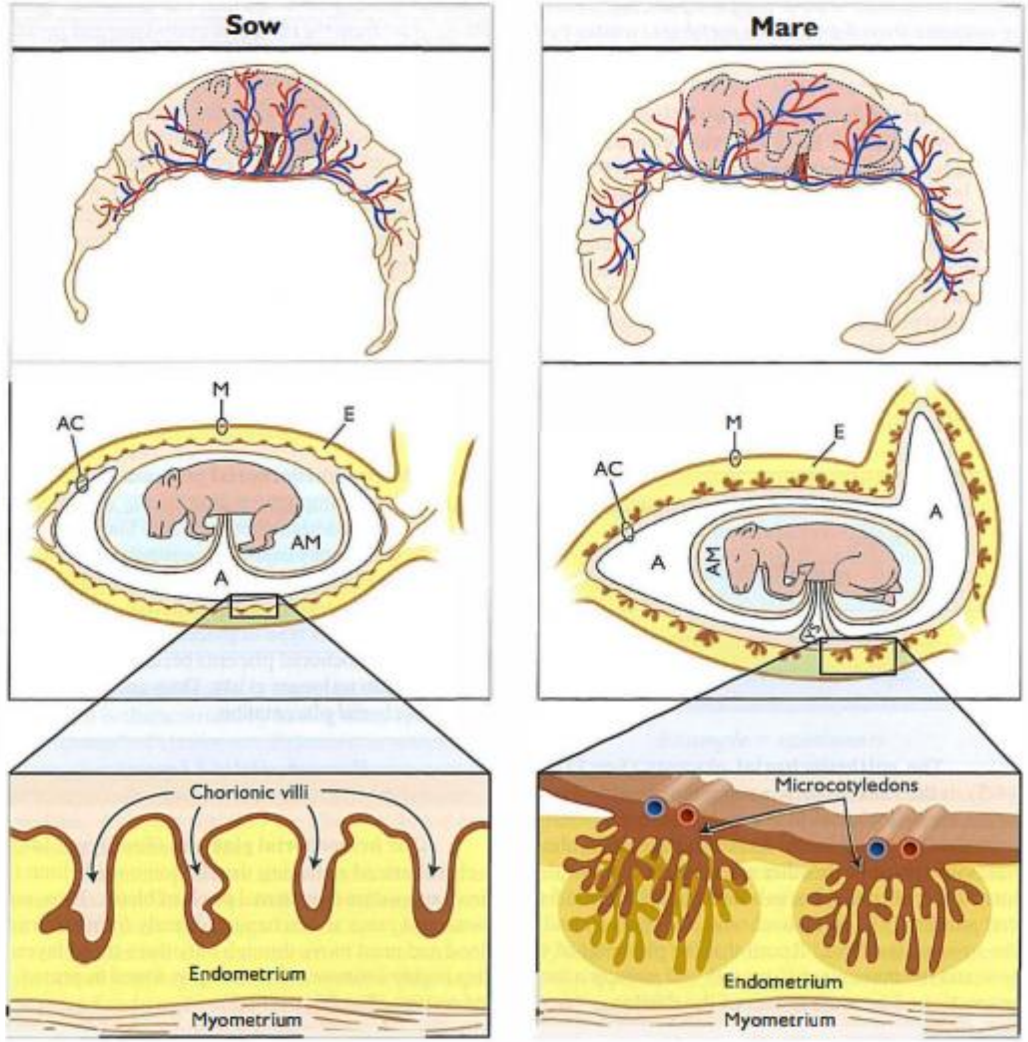
XII

- The conceptus consists of the embryo and the extraembryonic membranes (amnion, allantois and chorion).
- The functional unit of the fetal placenta is the chorionic villus. The chorionic villus is an "exchange apparatus" and provides increased surface area so that exchange is maximized.
- Placentas are classified according to the distribution of chorionic villi. These classifications are:
  - diffuse
  - zonary
  - discoid
  - cotyledonary

The Diffuse Placenta

XII

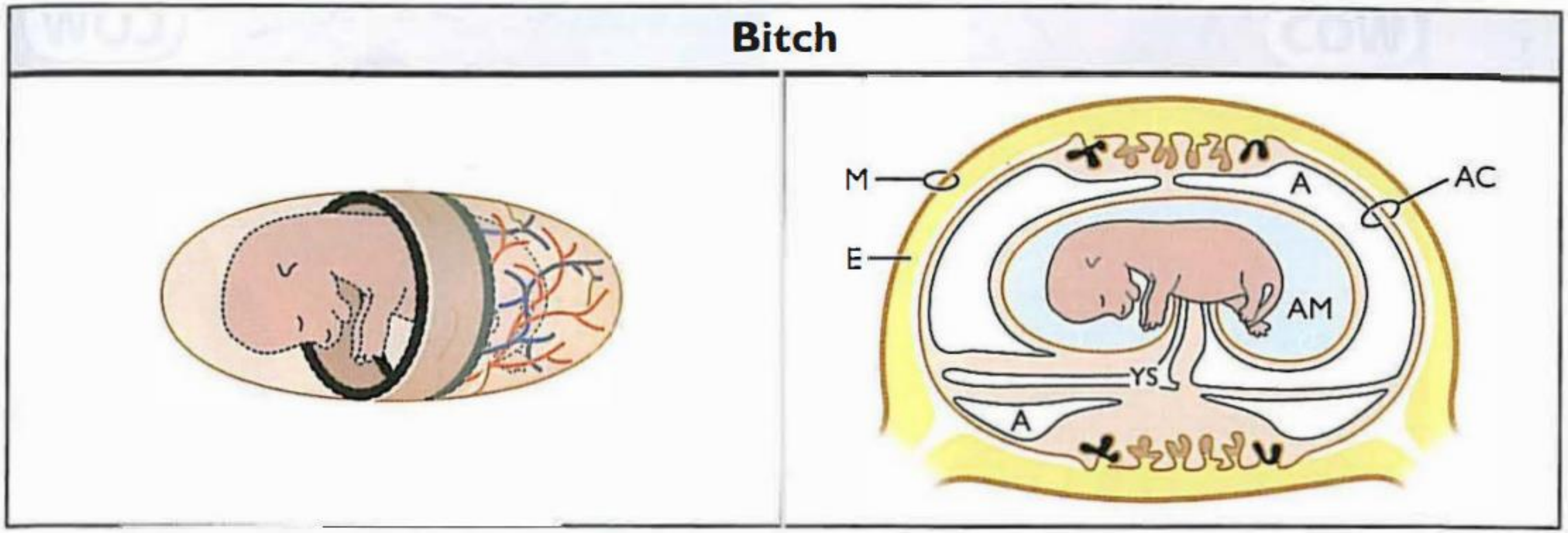
- Diffuse placentas have uniform distribution of chorionic villi that cover the surface of the chorion.

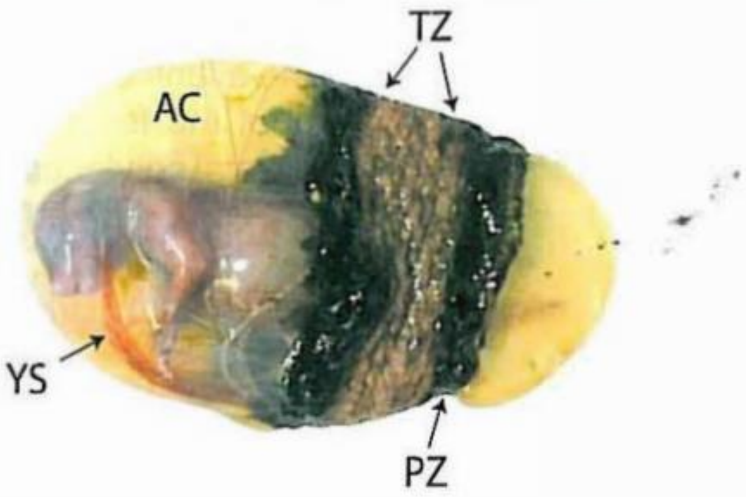


The diffuse placenta of the sow consists of many chorionic villi distributed over the entire surface of the chorion. They penetrate into the endometrium forming the fetal-maternal interface. Vessels from each chorionic villus merge and eventually form large vessels that enter the umbilical cord. A= Allantois, AC= Allantochorion, AM= Amnionic Cavity, E= Endometrium, M= Myometrium

The diffuse placenta of the mare consists of many microcotyledons distributed over the entire surface of the chorion. These microcotyledons are the site of fetal-maternal exchange. A= Allantois, AC= Allantochorion, AM= Amnionic Cavity, E= Endometrium, M= Myometrium, YS= Yolk Sac

The Zonary Placenta

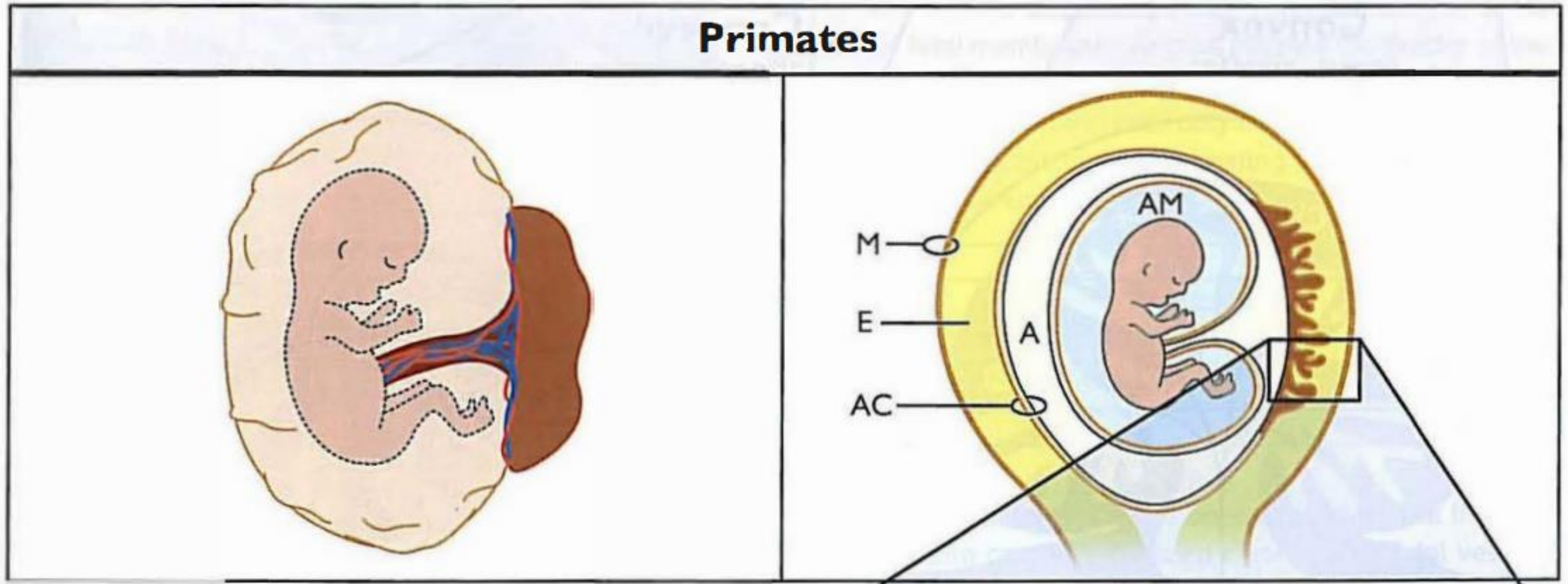


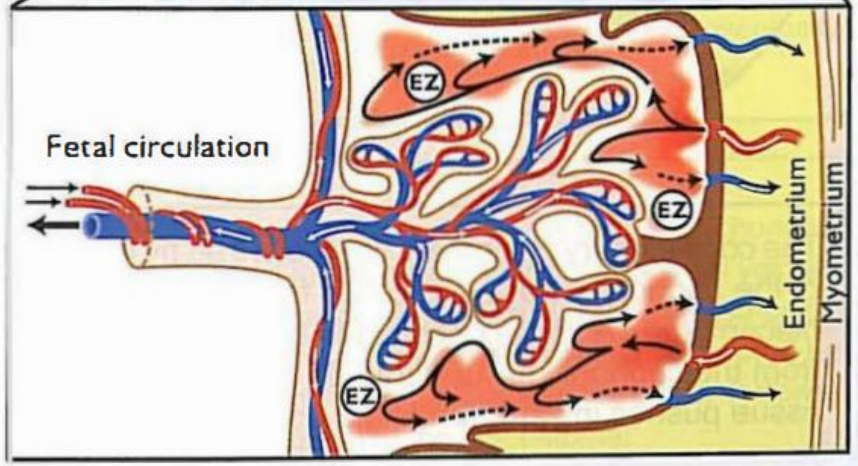


The zonary placenta consists of three distinct zones; a transfer zone (TZ), a pigmented zone (PZ) and a relatively nonvascular zone, the allantochorion (AC). In the zonary placenta, a band of tissue forms around the conceptus where nutrient transfer occurs. The pigmented zone (PZ) or paraplacenta represents local regions of maternal hemorrhage and necrosis.

A= Allantois, AC= Allantochorion, AM= Amnionic Cavity, E= Endometrium, M= Myometrium, YS= Yolk Sac

The Discoid Placenta



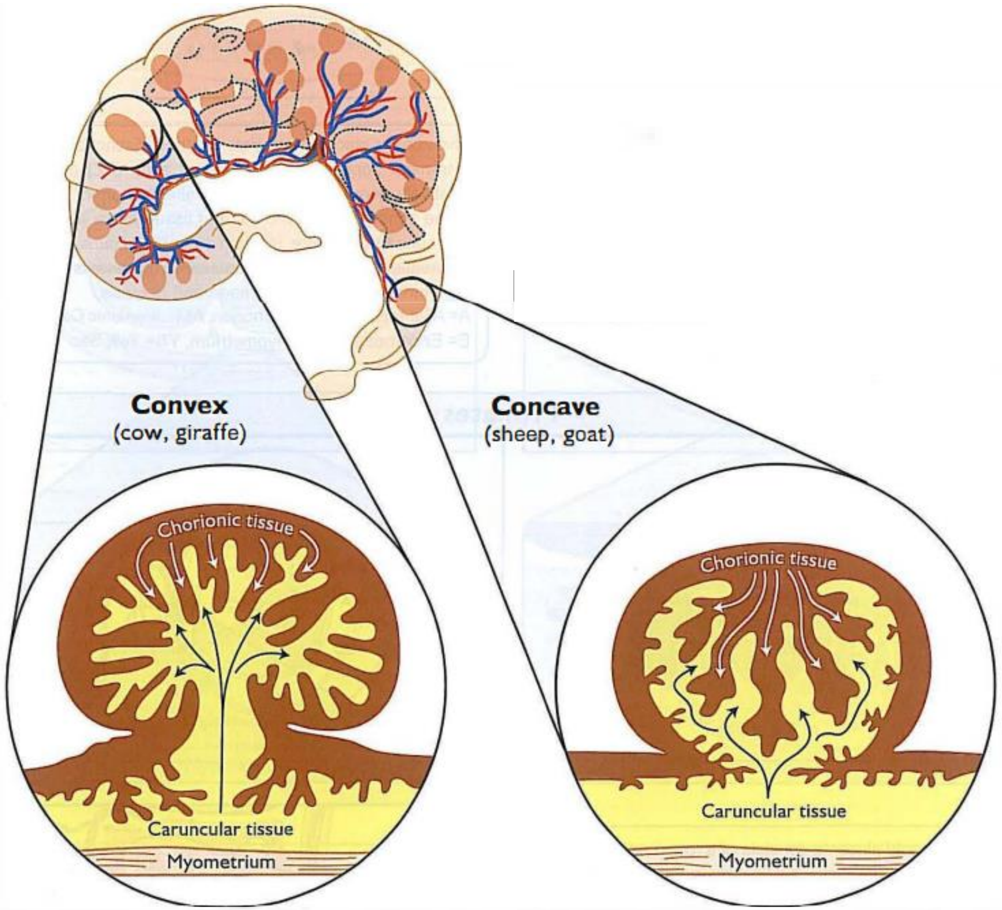


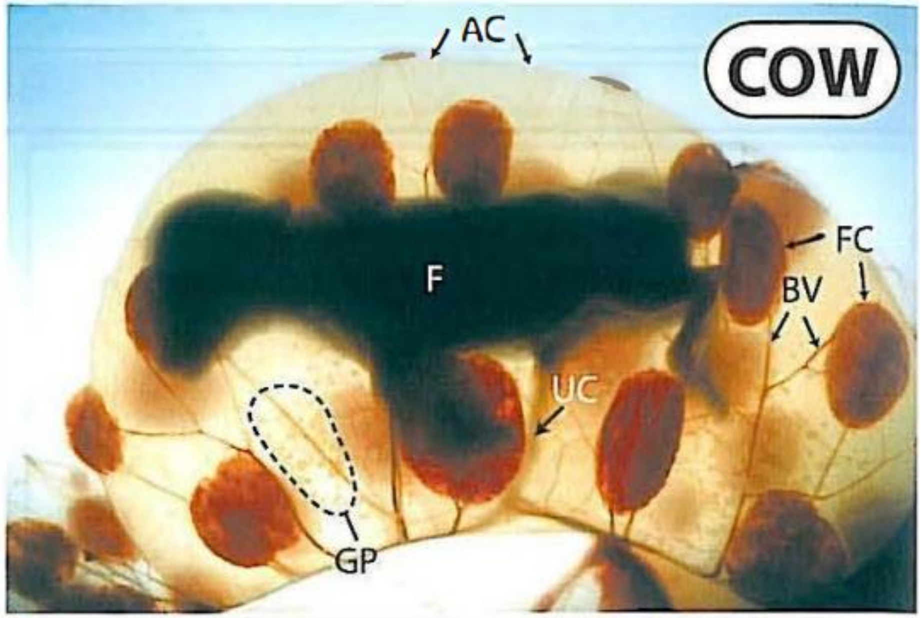
The discoid placenta consists of a round patch of chorionic tissue that forms the fetal-maternal interface. Vessels from the exchange zone merge to form the umbilical vessels that supply the fetus with blood. The vasculature of the chorion (within the disc) is immersed in pools of blood where metabolic exchange takes place.

A = Allantois, AC = Allantochorion,
AM = Amnionic Cavity, E = Endometrium,
EZ = Exchange Zone, M = Myometrium

The Cotyledonary Placenta

XII





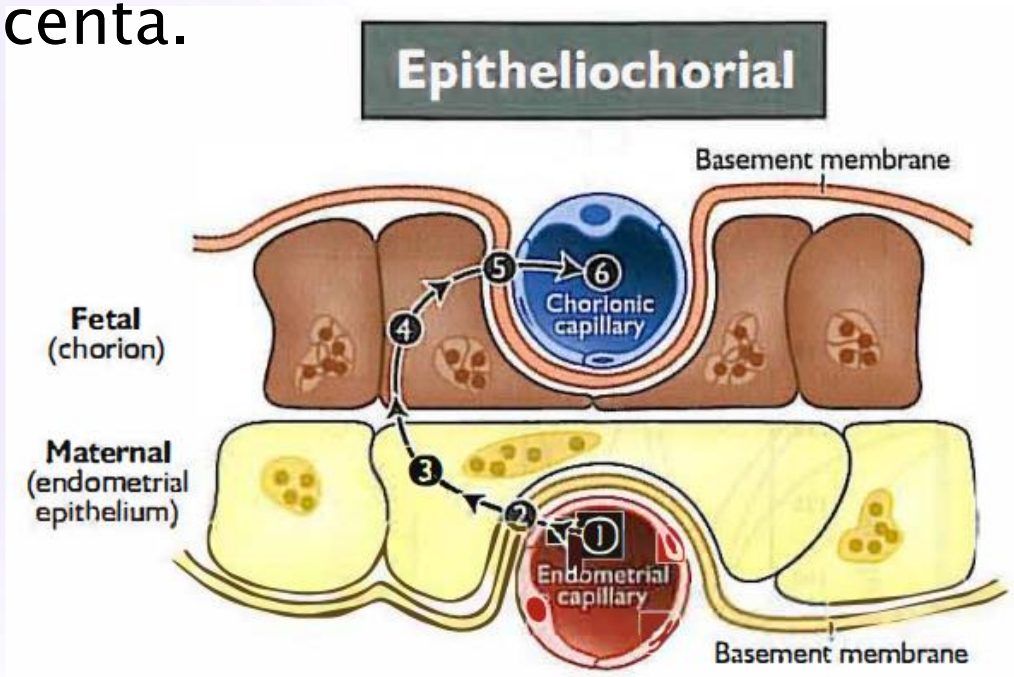
The cotyledonary placenta is characterized by numerous "button-like" structures distributed across the surface of the chorion. These are called fetal cotyledons. When they join with the maternal caruncle they form a placentome. A convex cotyledon becomes covered with the chorion. Many finger-like villi (red) originating from the chorionic tissue protrude toward the lumen of the uterus. In the concave cotyledon, the chorionic tissue pushes inward, forming a concave interface between the chorion and the maternal caruncle.

In the photograph above, the fetal membranes and the fetal cotyledons (FC) can be visualized. The membrane labeled AC is the allantochorion. The umbilical cord, (UC-arrow) of the fetus receives blood vessels (BV) from the fetal cotyledons (FC). Glycogen plaques (GP) can be visualized on the surface of the chorion and the amnion. These plaques are localized squamous proliferations called verrucae.

Microscopic Classification of Placenta

XII

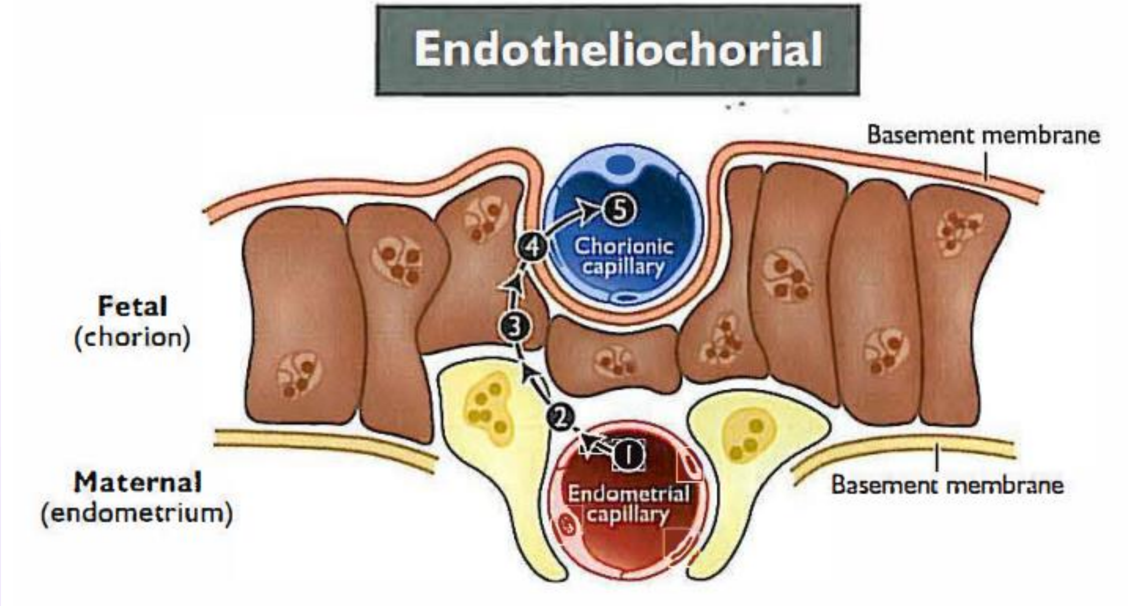
- Placental classification by microscopic appearance is based on the number of placental layers that separate the fetal blood from the maternal blood.
- The name of the placental type consists of a prefix describing the tissues of the maternal placenta and a suffix that constitutes the fetal tissue of the placenta.



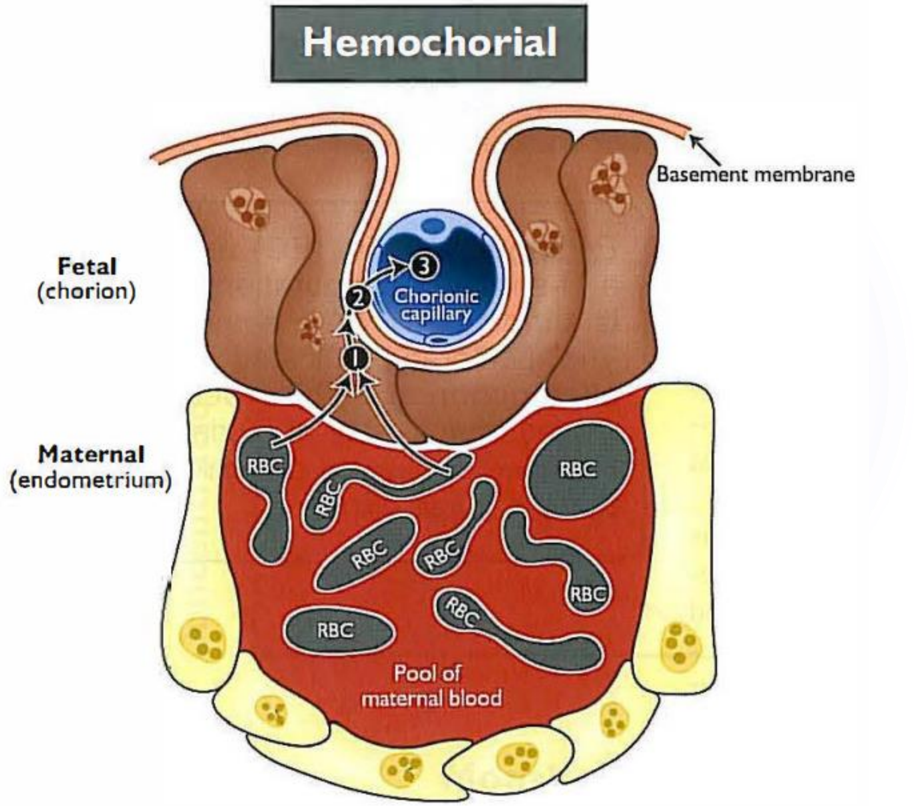
Epitheliochorial
(pigs, horses and ruminants)
6. Chorionic capillaries
5. Chorionic interstitium
4. Chorionic epithelium
3. Endometrial epithelium
2. Endometrial interstitium
1. Endometrial capillaries

Microscopic Classification of Placenta

XII



Endotheliochorial
(dogs and cats)
5. Chorionic capillaries
4. Chorionic interstitium
3. Chorionic epithelium
2. Endometrial interstitium
1. Endometrial capillaries



Hemochorial
(primates and rodents)
3. Chorionic capillaries
2. Chorionic interstitium
1. Chorionic epithelium
RBC= Red blood cell

Endocrine Role of Placenta

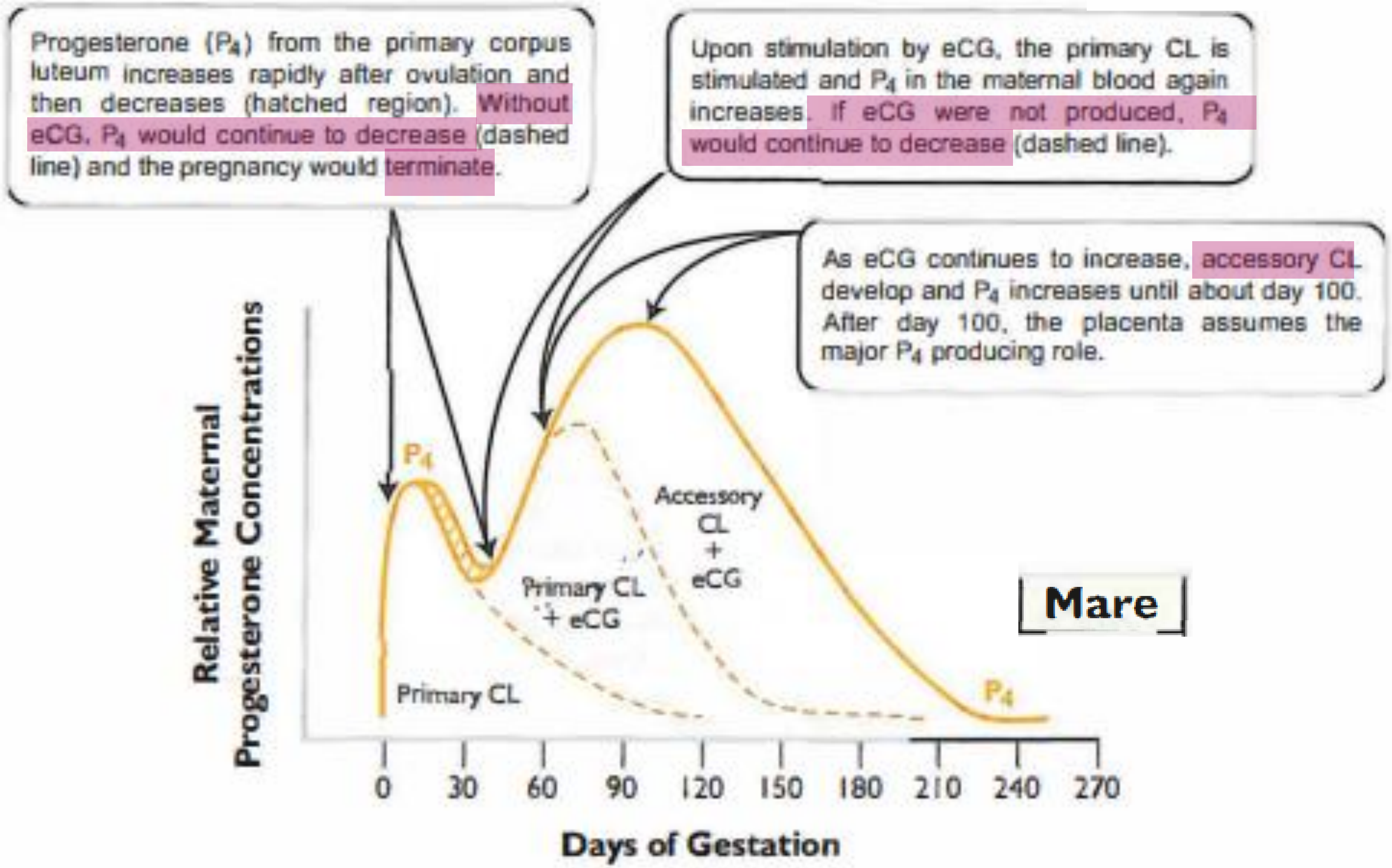
XII

- The placenta serves as a transitory endocrine organ.

1. equine Chorionic Gonadotropin (eCG) or pregnant mare's serum gonadotropin (PMSG):
   - produced by the endometrial cups of the placenta
   - acts as a luteotropin and provides a stimulus for maintenance of the primary corpus luteum.
   - responsible for controlling the formation and maintenance of supplementary (accessory) corpora lutea which leads to additional progesterone secretion.
   - has powerful FSH-like actions when administered to females of other species, and will cause marked follicular development in most species.
     - It is used commonly to induce superovulation where embryo transfer is performed (cow, sheep, rabbit but not mare).

Endocrine Role of Placenta

XII



Endocrine Role of Placenta

XII

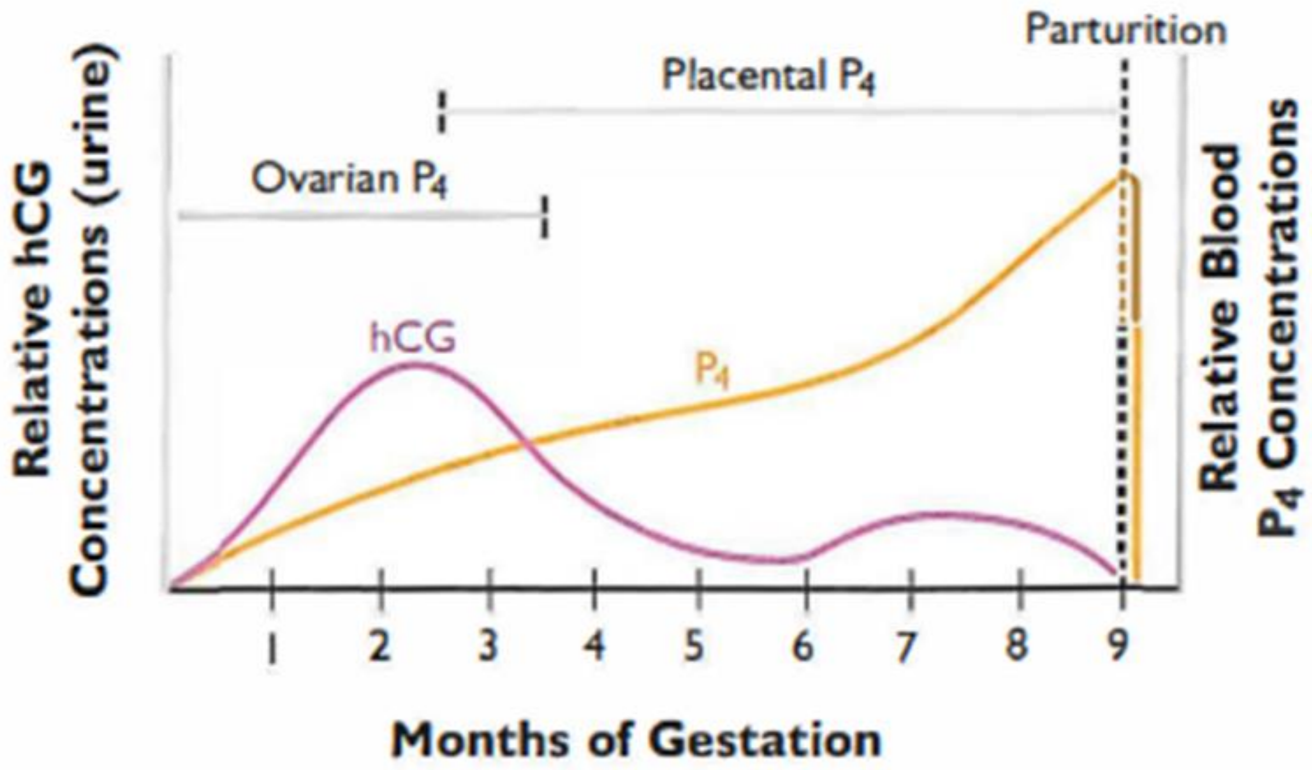
2. human Chorionic Gonadotropin (hCG). This hormone is not only found in the human but in many other primates.
   - It originates from the trophoblastic cells of the chorion and is secreted as soon as the blastocyst hatches from the zona pellucida.
   - It can be detected in the blood and urine of the pregnant woman as early as days 8 to 10 of gestation.
   - It increases rapidly in the urine of the pregnant woman, reaching a maximum value at about 2.5 months.
   - The primary role of hCG during early pregnancy is to provide a luteotropic stimulus for the ovulatory corpus luteum as it transitions into the CL of pregnancy.
   - Administration of hCG to non-primate females can cause ovulation.

Endocrine Role of Placenta

XII

Human chorionic gonadotropin peaks at about 2.5 months of gestation and then declines. This period of time is critical for maintenance of pregnancy because the corpus luteum assumes primary responsibility for progesterone secretion.

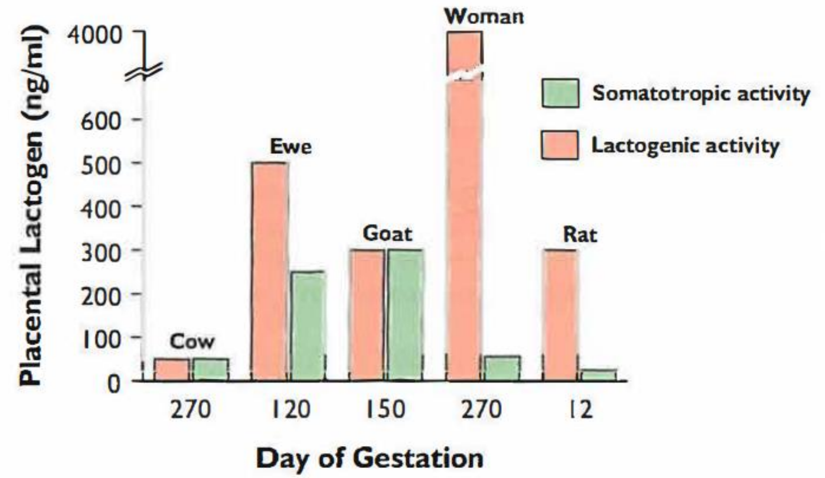
At about 2.5 to 3 months of gestation the placenta begins to assume the primary responsibility for progesterone secretion and continues this role until the time of parturition. hCG increases slightly between months 6 and 9 because of the increased placental mass.



Endocrine Role of Placenta

XII

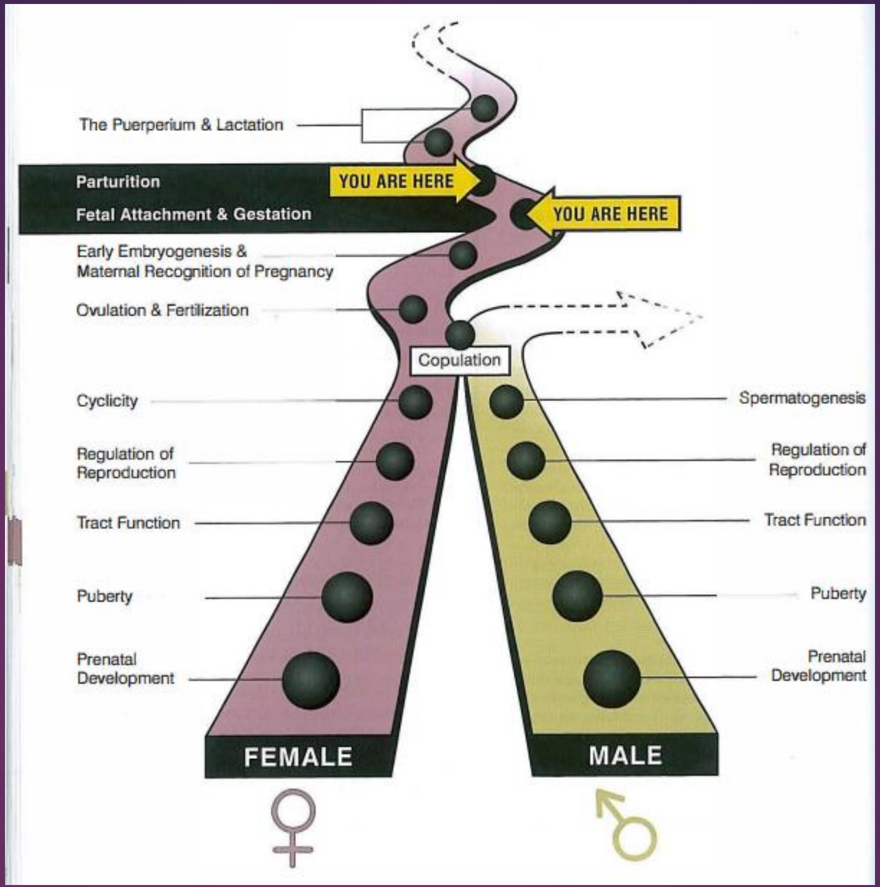
3. Placental lactogen that is also called somatomammotropin. They are believed to be similar to growth hormone, thus promoting the growth of the fetus. Placental lactogen also stimulates the mammary gland (lactogenic) of the dam.



Placental lactogen has both lactogenic actions and somatotrophic actions. The lactogenic activity of placental lactogen promotes mammary function in the dam, while the somatotropic activity promotes fetal growth.

4. Placental relaxin is secreted in humans, mares, cats, dogs, pigs, rabbits and monkeys. Its function is to cause softening and "relaxation" of the pelvic ligaments to facilitate expulsion of the fetus.

- Maternal blood relaxin levels are the basis for a commercial pregnancy diagnostic test at about 30 days of gestation in the bitch.



Section XIII

Parturition

Parturition

XIII

Parturition is a Complex Cascade of Physiologic Events

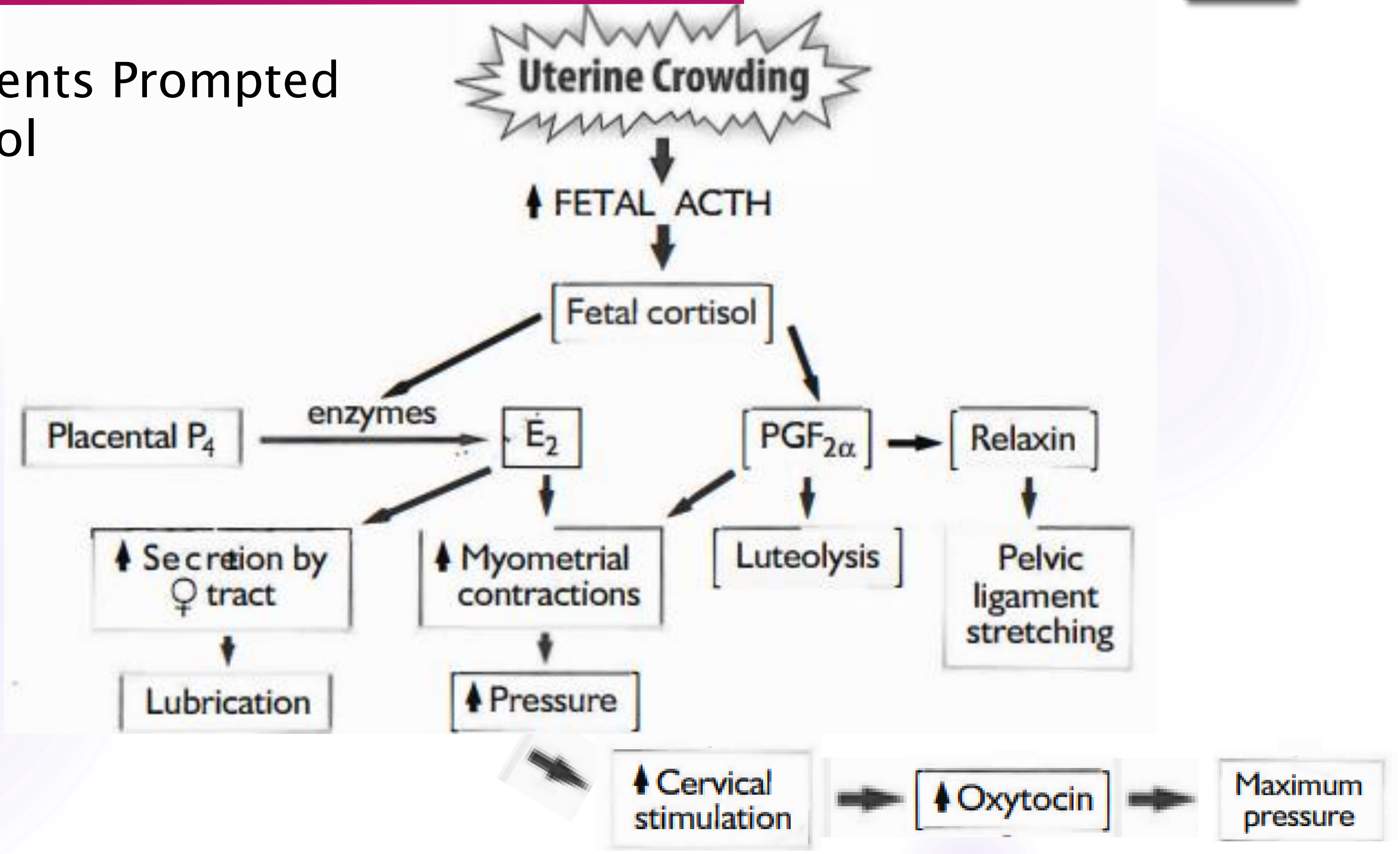
- The fetus triggers the onset of parturition:
  - As the fetus grows enough, space limitation causes adrenal corticotropin (ACTH) to be secreted by the fetal pituitary.
  - adrenal corticoids from the fetal adrenal cortex is then secreted.
    - 1) removal of the myometrial "progesterone block," enabling myometrial contractions to begin by
      - converting progesterone to estradiol.
      - Synthesis of $PGF_{2\alpha}$ which increases the myometrial contraction and regression of CL.
    - 2) increased reproductive tract secretions, particularly by the cervix.

Parturition

- The three stages of parturition are:
  - Stage I: initiation of myometrial contractions (removal of progesterone block)
  - Stage II: expulsion of the fetus
  - Stage III: expulsion of the fetal membranes
- The fetus initiates Stage I of parturition.
- Expulsion of fetus (Stage II) requires strong myometrial and abdominal muscle contractions.
- Expulsion of fetal membranes (Stage III) requires myometrial contractions.

Parturition

- Cascade of Events Prompted by Fetal Cortisol

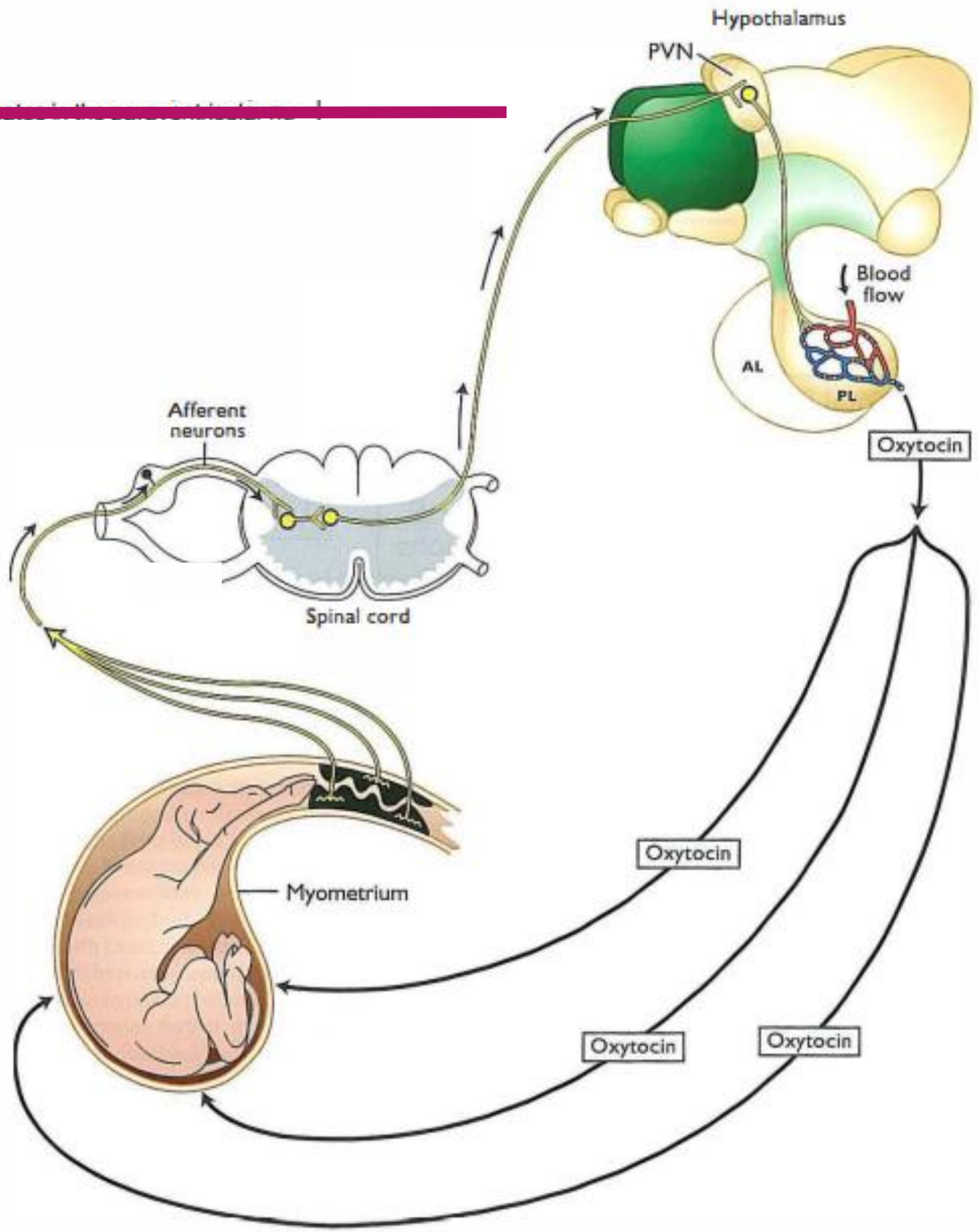


Parturition

XIII

1. Pressure on the cervix brought about by increased myometrial contractions activates pressure-sensitive neurons located in the cervix which eventually leads to oxytocin secretion

As the fetus moves through the birth canal, elevated pressure on the cervix stimulates sensory neurons. A neural pathway terminates in the paraventricular nucleus (PVN) and causes oxytocin to be secreted from the posterior pituitary lobe. Oxytocin stimulates contraction of the myometrium.



Parturition

XIII

2. Another important hormone involved in successful parturition is relaxin.
    - It is produced by either the corpus luteum or the placenta, depending upon the species.
    - The synthesis of relaxin is stimulated by $PGF_{2\alpha}$.
    - Relaxin causes a softening of the connective tissue in the cervix and promotes elasticity of the pelvic ligaments.
3. Estradiol initiates secretory activity of the reproductive tract in general and particularly the cervix to produce mucus prior to parturition.
    - This mucus washes out the cervical seal of pregnancy and thoroughly lubricates the cervical canal and the vagina.

Parturition

XIII

- As myometrial contractions continue to increase, the feet and head of the fetus begin to put pressure on the fetal membranes.
  - When the pressure reaches a certain level, the membranes rupture, with subsequent loss of amniotic and allantoic fluid. This fluid also serves to lubricate the birth canal.
- As the fetus enters the birth canal, it becomes hypoxic (deprived of adequate levels of oxygen). This hypoxia promotes fetal movement that, in turn, promotes further myometrial contraction with a positive feedback system which reduces the time of parturition because an increased strength of contraction follows fetal movement.
- In a sense, the fetus is controlling its exit from the uterus. The uterine contractions are accompanied by abdominal muscle contractions of the dam that further aid in expulsion of the fetus.

Parturition

XIII

Species	Stage I (Myometrial Contractions/ Cervical Dilation)	Stage II (Fetal Expulsion)	Stage III (Fetal Membrane Expulsion)
Alpaca	2 to 6h	5 to 90 min	45 to 180 min
Bitch	6 to 12h	6h (24h in large litters)	most placentas pass with neonate or within 15 min of birth
Camel	3 to 48h	5 to 45 min	40 min
Cow	2 to 6h	30 to 60 min	6 to 12h
Ewe	2 to 6h	30 to 120 min	5 to 8h
Llama	2 to 6h	5 to 90 min	45 to 180 min
Mare	1 to 4h	12 to 30 min	1h
Sow	2 to 12h	150 to 180 min	1 to 4h
Queen	4 to 42h	4 kittens/litter, 30-60 min/kitten	most placentas pass with neonate
Woman	8+h	2h	1h or less

Dystocia

XIII

- Prolonged duration of each stage in parturition is called dystocia which may result in serious complications to both the fetus and the dam.
- Difficulties in parturition usually occur in the second stage (expulsion of the fetus):
  1. excessive size of the fetus
  2. failure of proper fetal rotation
     - About 5% of all births in cattle are characterized by abnormal positioning of the fetus during parturition.
  3. multiple births in monotocous species.
     - I) both twins may be presented simultaneously,
     - 2) the first fetus is positioned abnormally and therefore blocks the second or
     - 3) the uterus becomes fatigued by difficult and sustained contractions

Retained Placenta

- Myometrial contractions continue after expulsion of the fetus although they are not as strong (stage III of parturition).
  - These contractions are responsible for expelling the placenta.
- Retention of the fetal membranes (also referred to as "retained placenta"), occur in 5-15% of parturitions in healthy dairy cows.
- The underlying cause of retained placenta appears to be that placental connective tissue is not enzymatically degraded by cotyledonary proteolytic enzymes. Thus, fetal cotyledons remain attached to maternal cotyledons.
- Retained placenta is rare in mares, sows, bitches and queens.

Good Luck!