

Female Reproduction

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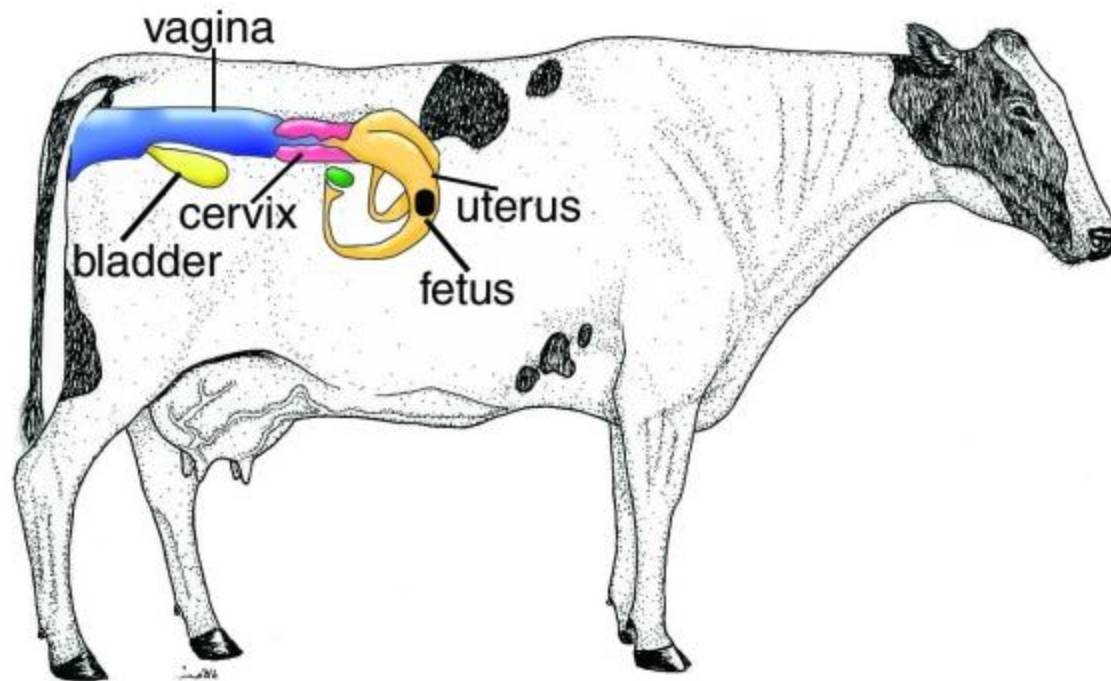
Reproduction

Ability of animal to produce
a new generation and
maintenance of the species

The female reproductive system consists of :

- Ovaries(exocrine &endocrine function)
- Oviducts or fallopian tubes which transmit the ova to the uterus
- Uterus
- Vagina
- External genitalia(vulva)
- Accessory glands(mammary glands)

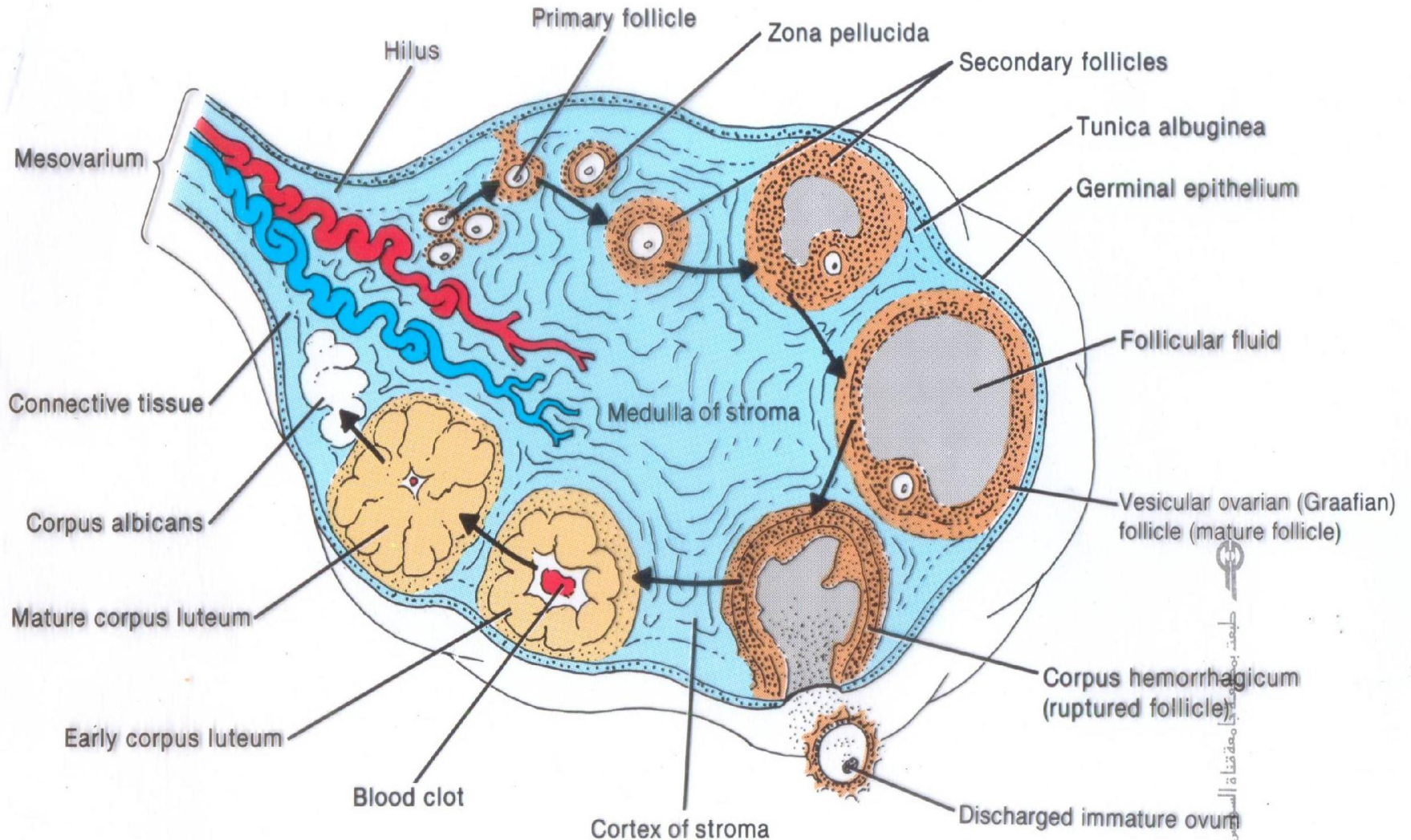
Reproductive System



Ovaries

- Paired glands(unshelled almonds in size and shape)
- Positioned in the pelvic cavity, one on each side of the uterus.
- They are maintained in position by a series of ligaments(suspensory ligament, mesovarium and ovarian ligament)

Microscopic structure of the ovary



Fallopian tubes:

Two uterine tubes(oviducts) extend laterally from the uterus and transport ova from the ovaries to the uterus.

Fallopian tubes consisted of:

Infundibulum (funnel shaped), trap the ova, surrounded by fimbriae.

Ampulla (site of fertilization).

Isthmus (short, narrow thick walled).

Uterus:

Site of implantation of fertilized ova and development of the fetus.

It consists of: (horns -- body-- isthmus -- cervix).

The interior of the body (**uterine cavity**)

The interior of the cervix (**cervical canal**)

The junction between the isthmus with the cervical canal is the **internal os**.

The **external os** is the place where the cervix opens into the vagina.

Vagina:

- Serves as a passage way for the vaginal secretions, receptacle for penis during coitus ,It is the lower portion of the birth canal.

- Musculo-tubular organ:**

- The **muscularis** is composed of **long.S.M.** that can **stretch**. This distension is important because the vagina receives the penis during sexual intercourse and serves as the lower portion of the birth canal.

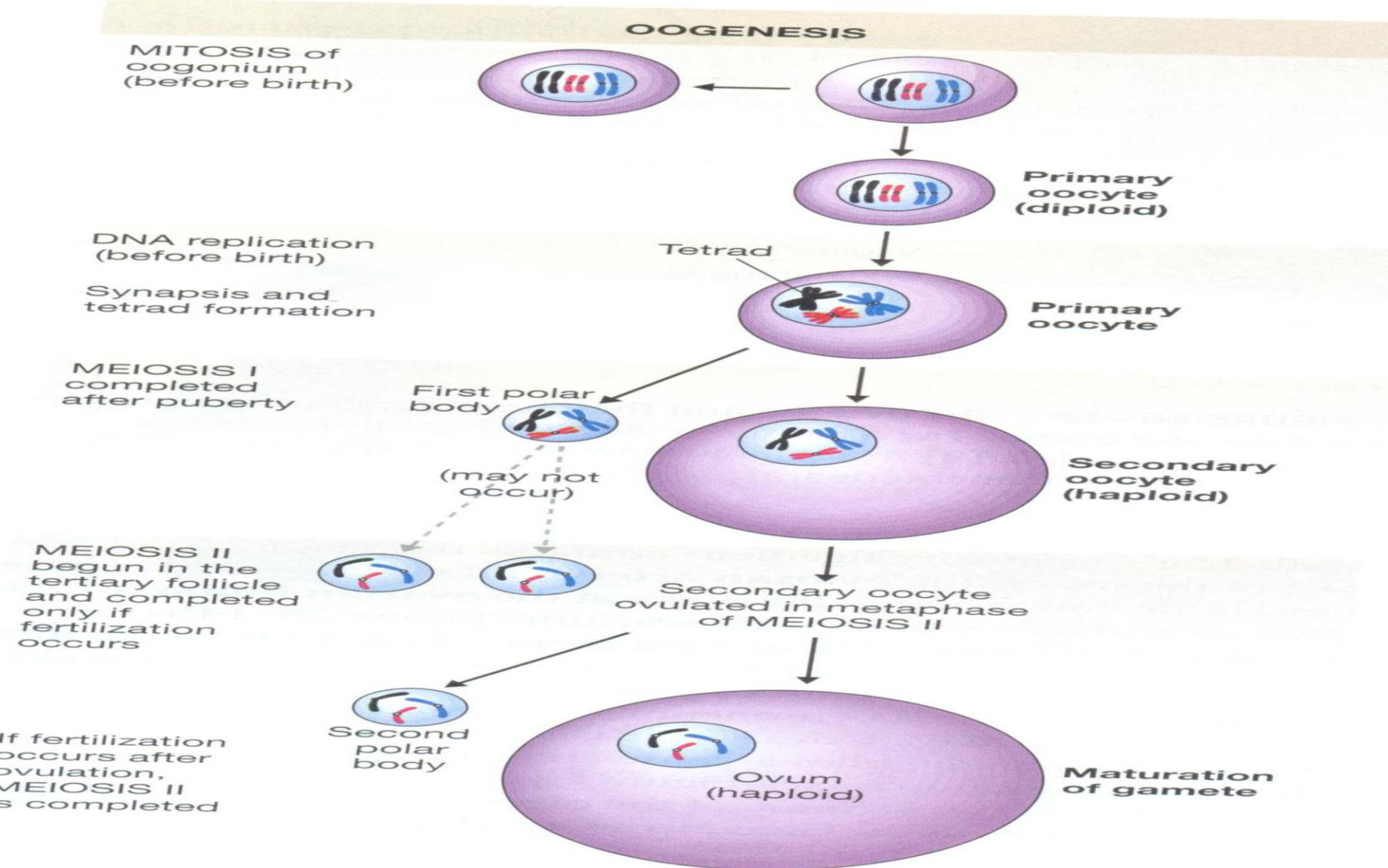
- The **mucosa** of the vagina contains large amounts of **glycogen**, On **decomposition** , it produces **organic acids (low pH)** which retards microbial growth, injurious to sperm cells but semen neutralizes this acidity to ensure survival of the sperm.

- Hymen:** thin fold of vascularized m.m forms a border around the orifice partially closing it.

The exocrine function of the ovary is oogenesis

- In embryo, the oogonia divide rapidly from the second to seventh month of **gestation** to form **7 million germ cells** .
- The number of germ cells drops to **2 millions** and still till **birth**.
- Most oogonia die during this period while the remaining enter the first meiotic division (primary oocyte).
- **At puberty 300 000** of oocyte enter meiosis .

Oogenesis: is the process by which mature oocyte (that is competent for fertilization,) is produced.



During first meiotic

❖ One of daughter cell contains hardly cytoplasm (**first polar body**).

❖ The other cell has entire volume of cellular constituents (**secondary oocytes**).

During second meiotic division mature ovum and second polar body are produced .

Puberty

It is the time at which cyclic gonadal function begins. Onset of the **first estrous** cycle and **sexual desire** under the control of C.N.S. and gonadotropins.

The age of puberty is:-

Cows	9-12 months,
Buffaloes	15- 20 months,
Sheep & goats	4-8months,
Mares,	10-12 months,
Cats	7 months,
Bitches	9-14 months.

Theories of puberty:

1-Small amounts of **estrogen** are secreted by the ovaries **before puberty** and hold up gonadotropin secretion.

2-**Pineal gland secretes melatonin before puberty** which **inhibits GnRH** from the hypothalamus . Its activity gradually diminished as the animal approaches puberty. This leads to an increase in the output of GnRH from hypothalamus and gonadotropins from the interior pituitary gland .

3-**Thymus gland** contributes with the **pineal gland** in inhibiting gonadotropin secretion .

4- Before puberty, the brain is very sensitive to the inhibiting effects on gonadotropin secretion

Control of onset of puberty

1-Hereditary factors:

- ❖ Uni or bilateral ovarian hypoplasia
- ❖ Aplasia of duct system

2-Nutritional factors .

Protein, carbohydrate, fat ,vitamin and mineral.

3-Environmental factors.

4-**Sex**:earlier in female human but earlier in male in buffaloes and cattle.

5-**Endocrine factors** : maturation of CNS and subsequently maturation of hypothalamus lead to release of GnRH lead to Gn lead to steroid release which is responsible for onset of puberty (control growth of genitalia and sexual behavior and gametogenesis)

Types of puberty:

1-Normal

2- Early (precocious :

A-pseudo puberty : development of secondary sexual characters without gametogenesis

B-True puberty

3-Delayed (absent)

Sexual maturity

Complete physical and physiological development of the reproductive tract following puberty by a certain time .

It is the suitable time to start pregnancy and parturition .

Female reproductive cycle

Definition

Certain changes occur in female reproductive tract in a cyclic manner controlled by gonadotropin (from ant. pituitary) and sex hormone (from gonads).

In human beings, it is called menstrual cycle.
In animals, it is called estrous cycle.

REPRODUCTIVE CYCLE

Estrous cycle in domestic animals

A. Ovarian Cycle

1. Follicular Phase

a- Oogenesis

b- Folliculogenesis

2. Ovulation

3. Luteal Phase (Luteonization or Luteolysis)

B. Interplay between Neuro-endocrine factors in controlling the ovarian and reproductive cycles.

C. Pregnancy Events including:

(1) Fertilization

(2) Maternal recognition of the conceptus

(3) Embryonic development and differentiation

(4) Implantation

(5) Placentation

D. Parturition

E. Lactation

Oogenesis:

It is the process by which a mature oocyte that is competent for fertilization, is produced.

Folliculogenesis:

It is the process by which mature follicles are produced.

These follicles play important roles in Steroidogenesis process by which steroid hormones, mainly estrogens are produced.

Ovulation:

It is the phase in which the dominant follicle (Graafian follicle) can ovulate releasing mature secondary oocyte, and the remaining cellular part changed to corpus luteum.

Luteonization:

It is the process by which corpus luteum is formed during early luteal phase.

Luteolysis:

It is the process by which the corpus luteum shrinks during:

Late luteal phase due to failure of fertilization.

Or at the end of gestation.

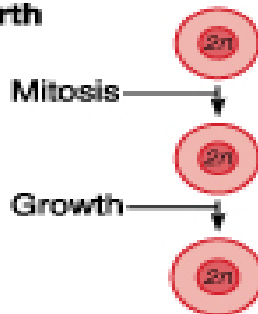
Oogenesis

Folliculogenesis

Melotic Events

Follicle Development In Ovary

Before birth



Oogonium (stem cell)

Primary oocyte

Primary oocyte (arrested in prophase I present at birth)

Childhood

(ovary inactive)



Primary oocyte (still arrested in prophase I)

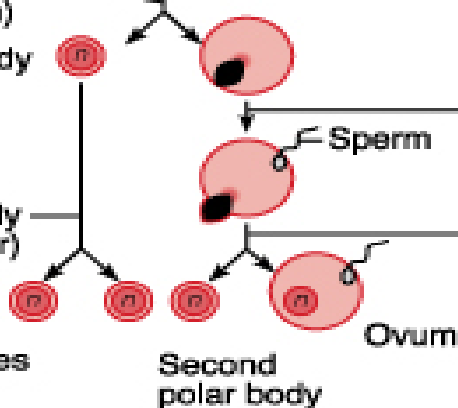
Spindle

Meiosis I (completed by one primary oocyte each month)

First polar body

Meiosis II of polar body (may or may not occur)

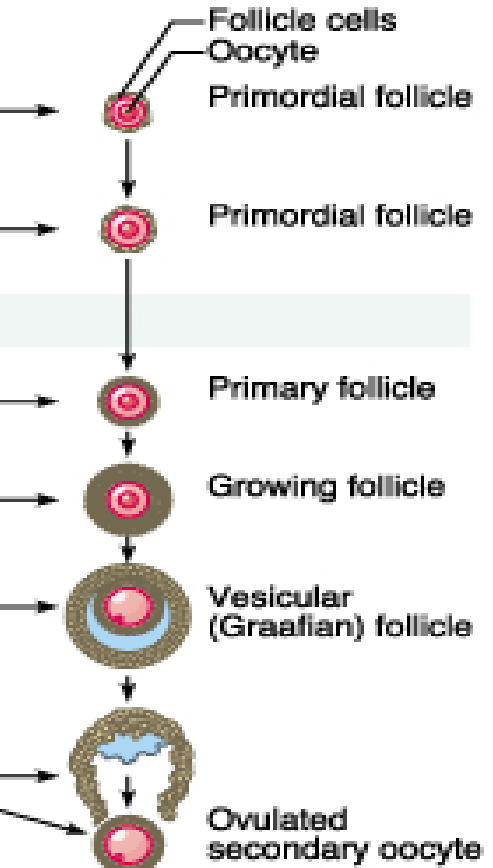
Polar bodies (all polar bodies degenerate)



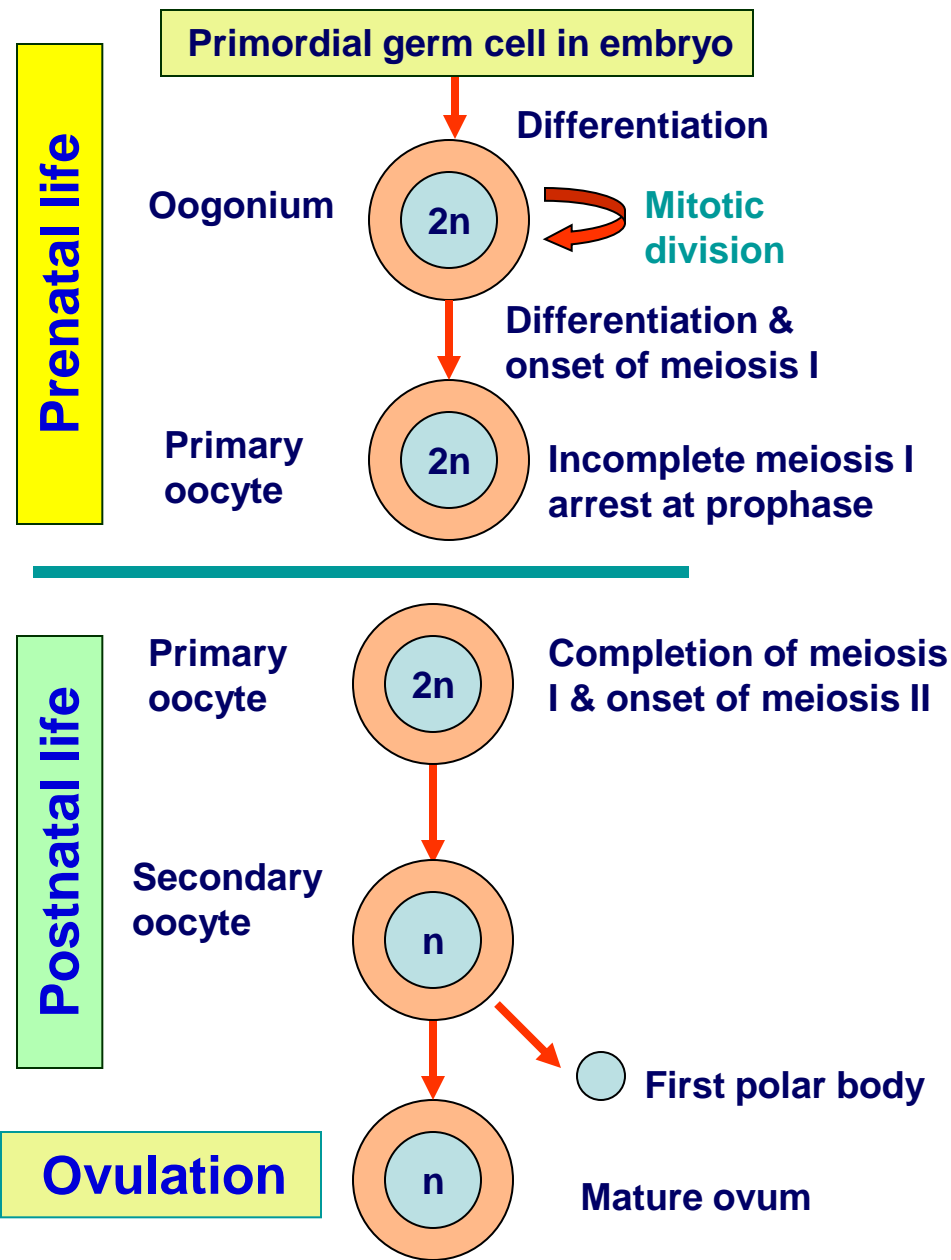
Secondary oocyte (arrested in metaphase II)

Ovulation

Meiosis II completed (only if sperm penetration occurs)



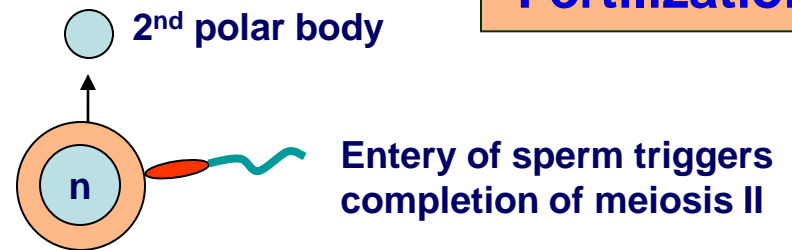
OOGENESIS IN MAMMALS



OOGENESIS differs from spermatogenesis in several ways. Whereas the gamete formed by spermatogenesis is essentially a motile nucleus, the gamete formed by oogenesis contains all the materials needed to initiate and maintain metabolism and development.

Therefore, in addition to forming a haploid nucleus, oogenesis also builds up a store of cytoplasmic enzymes, mRNAs, organelles and metabolic substrates that all are essential for the future **embryo** nourishment and development.

Fertilization



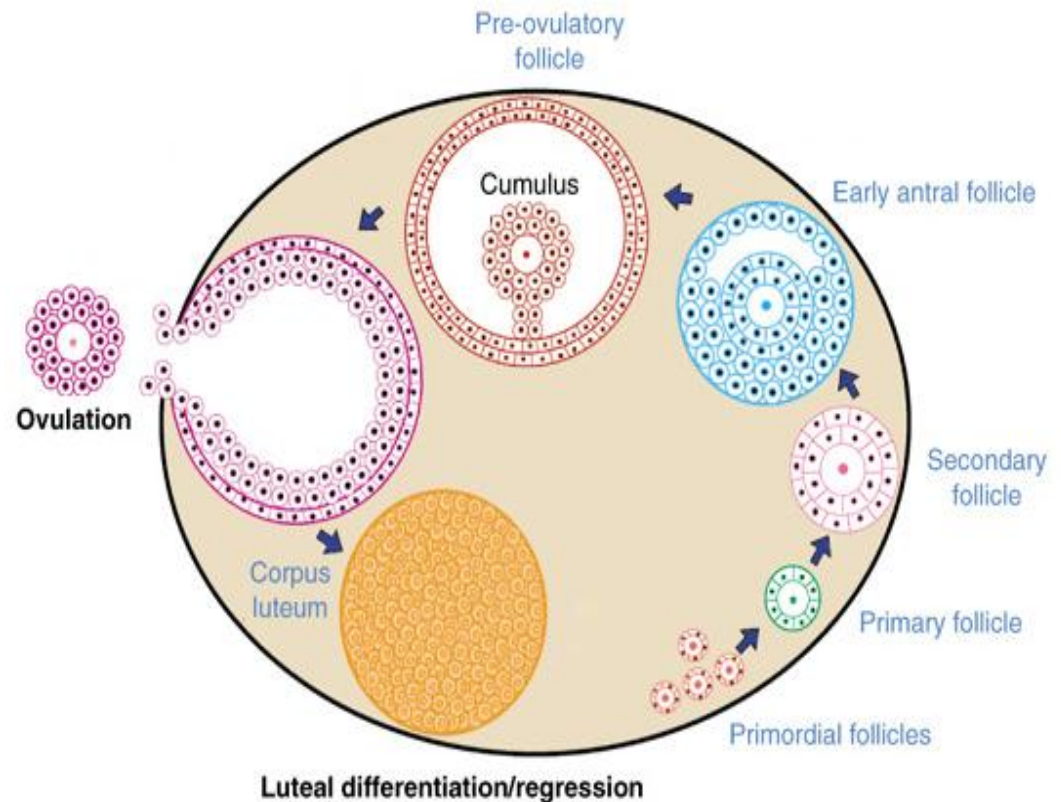
FOLLICULOGENESIS

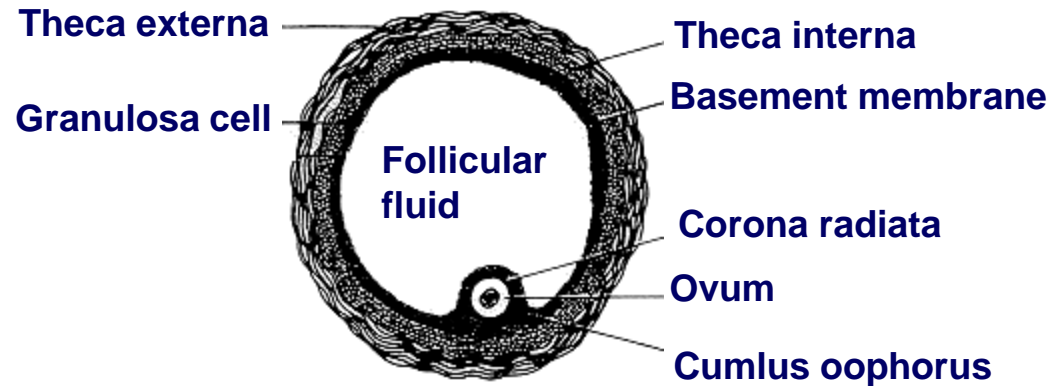
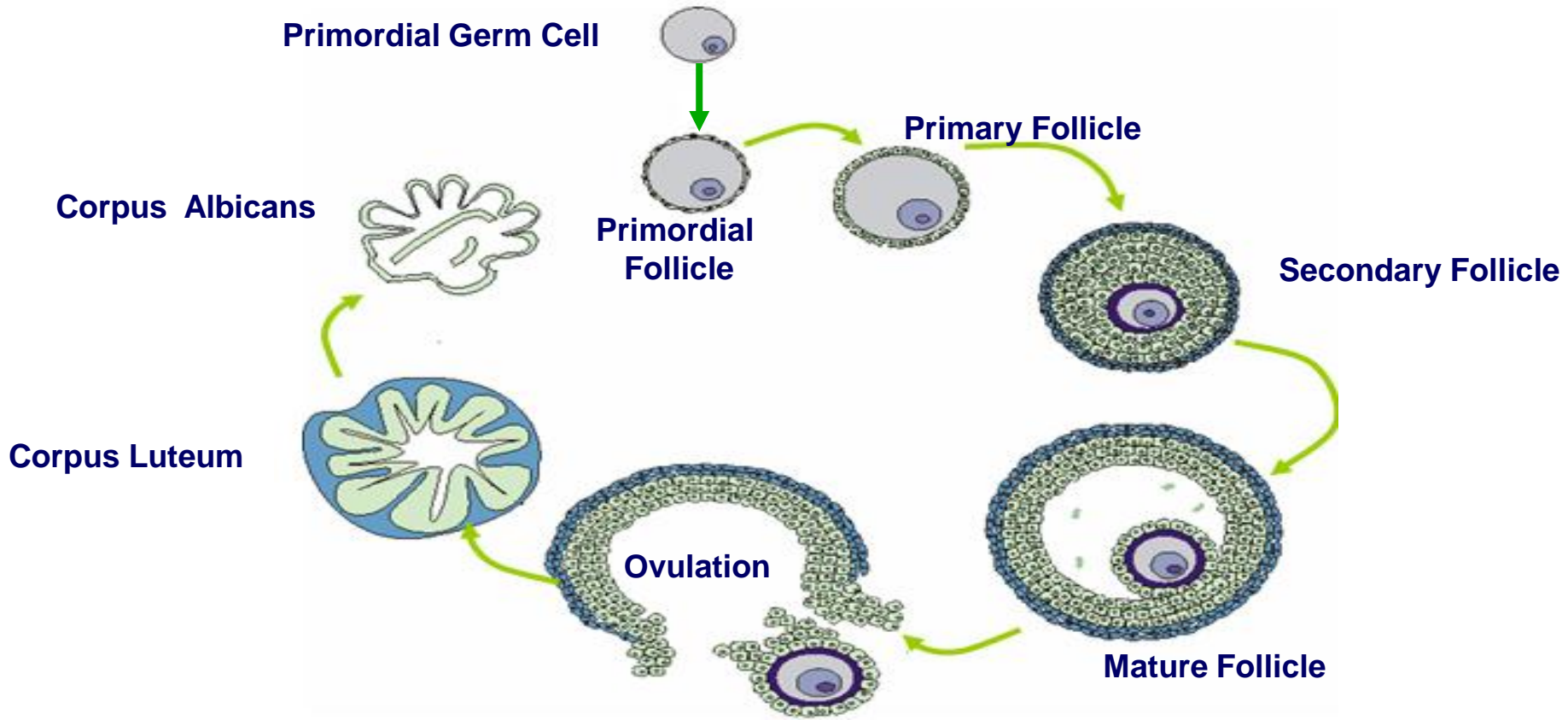
Ovary has both endocrine (produces hormones) and exocrine (release of the oocyte) function.

The female is born with ovaries containing a limited pool of ova. Folliculogenesis defined as the formation of Graafian follicle from a pool of primordial (non-growing) follicle.

Types of Ovarian Follicles:

Primordial Follicles: constitutes a centrally located oocyte and a single layer of flattened granulosa cells associating with the oocyte. The cell cycle of oocytes at this stage is arrested at the prophase of the first meiotic division, and oocytes usually are never released from the arrest until they have passed through a growth phase





Types of Ovarian Follicles

1- Primordial Follicle single layer of squamous epithelial cells resting state

3- Secondary follicle

primary oocyte
zona pellucida present
multiple layers of granulosa cells
thecal layer forms
pre-antral

5- Graafian follicle

latest stage of tertiary follicle
primary oocyte
final stage
preovulatory

Follicle growth involves hormonally induced proliferation and differentiation of both **theca** and **granulosa** cells leading to increased ability of follicles to produce **estradiol (E2)** and respond to **gonadotropins (LH & FSH)**

2- Primary follicle

single layer follicle cells
primary oocyte
follicle cells expand (cuboidal)

4- Antral follicle

Many layers of Granulosa cells
primary oocyte
oocyte reaches maximum size
granulosa cells expand
zona pellucida present
cavities appear, antrum forms

Oocyte numbers

- Fetal – 7,000,000
- Birth – 2,000,000
- Aged - 20,000
- Number ovulated
- >> human ~500 >> cow ~350

Follicles that produce E2 will gain **LH receptors** necessary for ovulation and luteinization

Folliculogenesis)

It is divided into 5 events:

Recruitment (initial ,cyclic) FSH↑

Common growth phase (FSH)↓

Deviation -

Selection -

Dominance

Recruitment=emergence: It is the process where a cohort of follicles begins to mature in a sufficient pituitary gonadotropins to permit progress towards ovulation.

it is corresponding to entry into terminal growth of a group of follicles. pituitary gonadotropic stimulation permit progress towards ovulation.

Common growth phase : the dominant follicle grows at a continuing rate , and the remaining or subordinate follicles regress or grow at a reduced rate and then regress .

It occurs after emergence of(7-11 follicles enter).

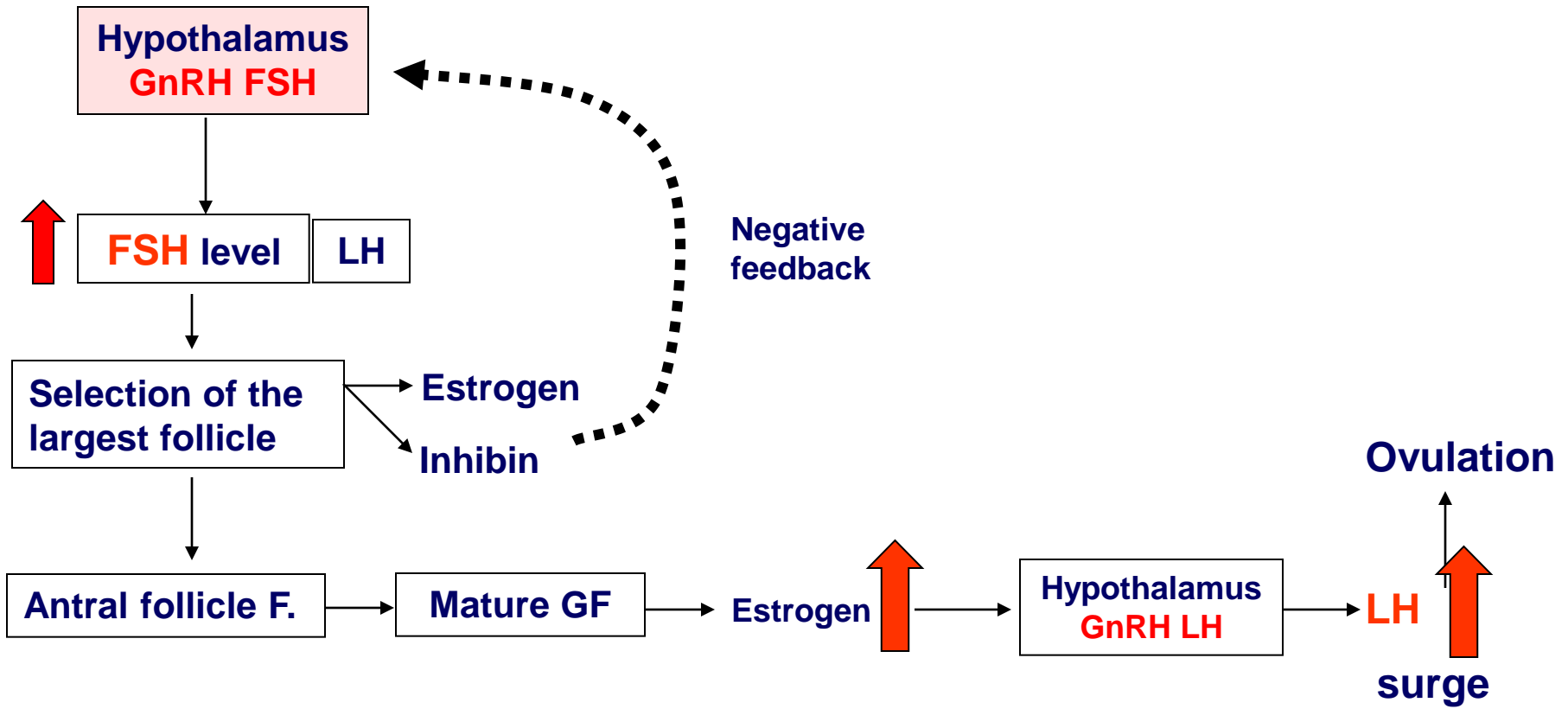
Higher levels of estrogen and inhibins are secreted from the largest follicle which suppress the pituitary FSH released during the mid follicular phase.

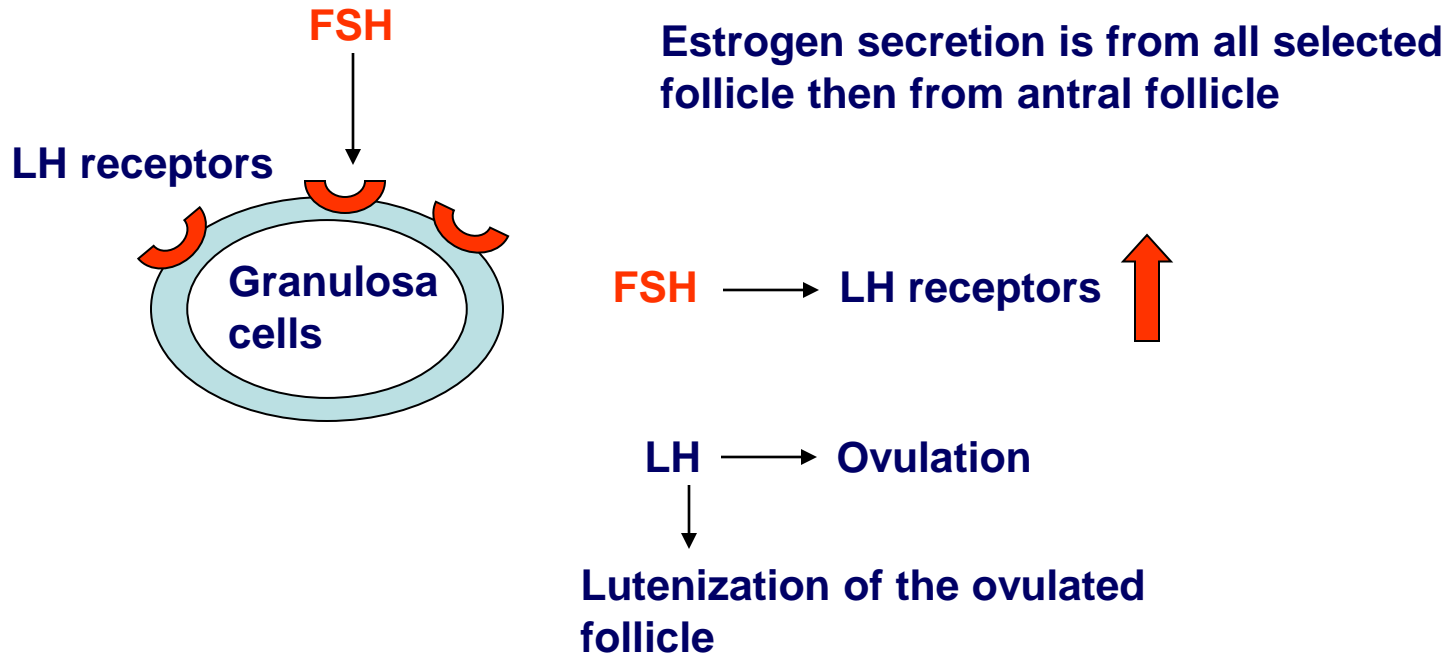
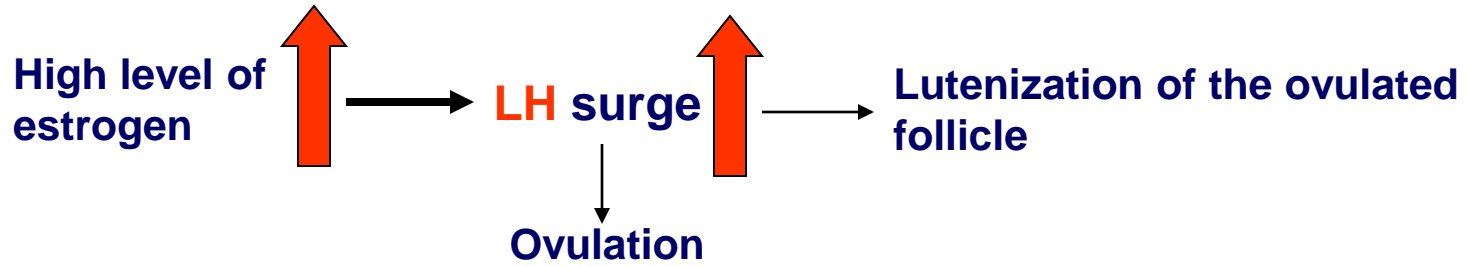
The growing follicles also produce higher levels of autocrine and paracrine growth factors that stimulate vasculature of the follicle.

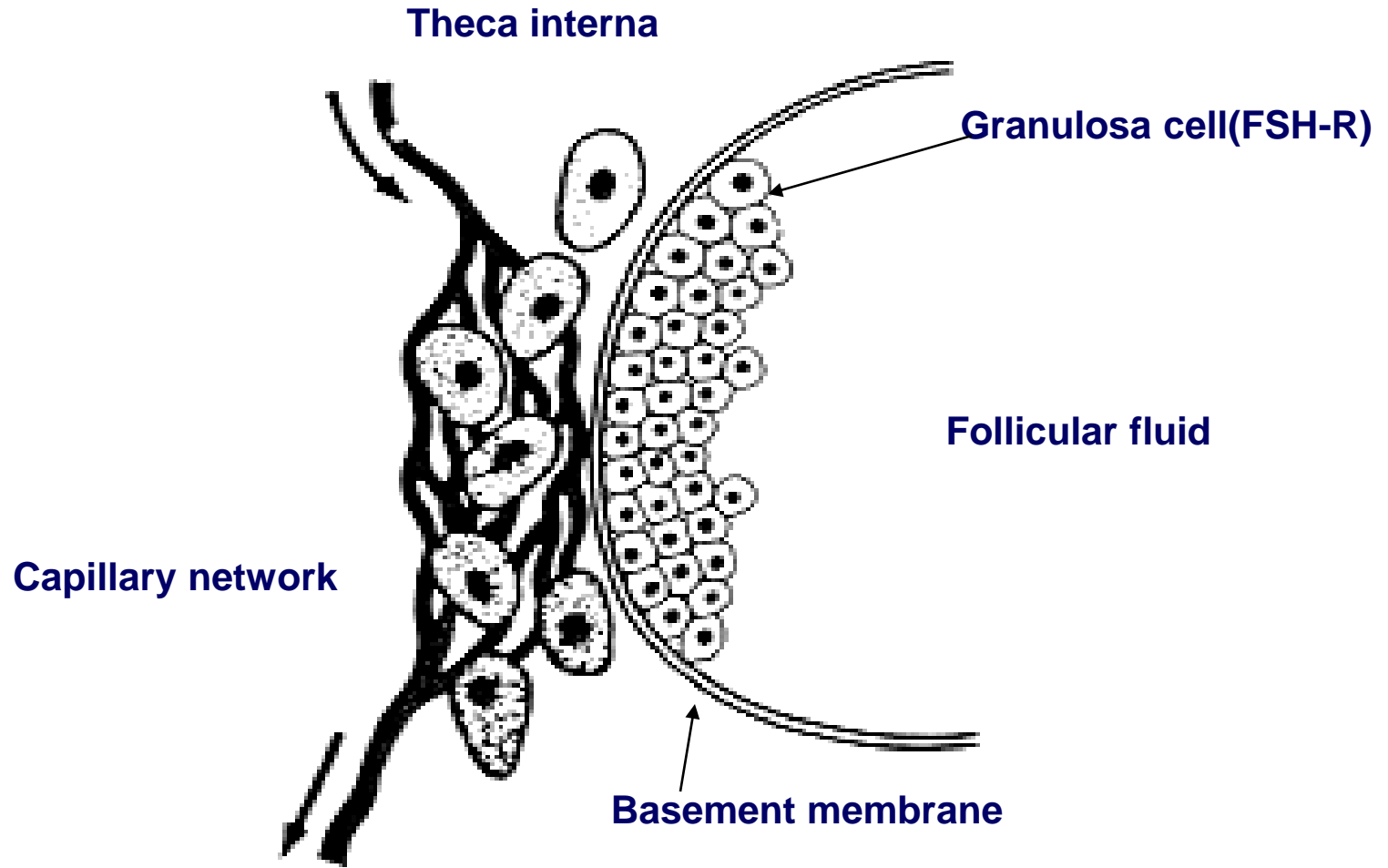
Endocrine control of reproduction



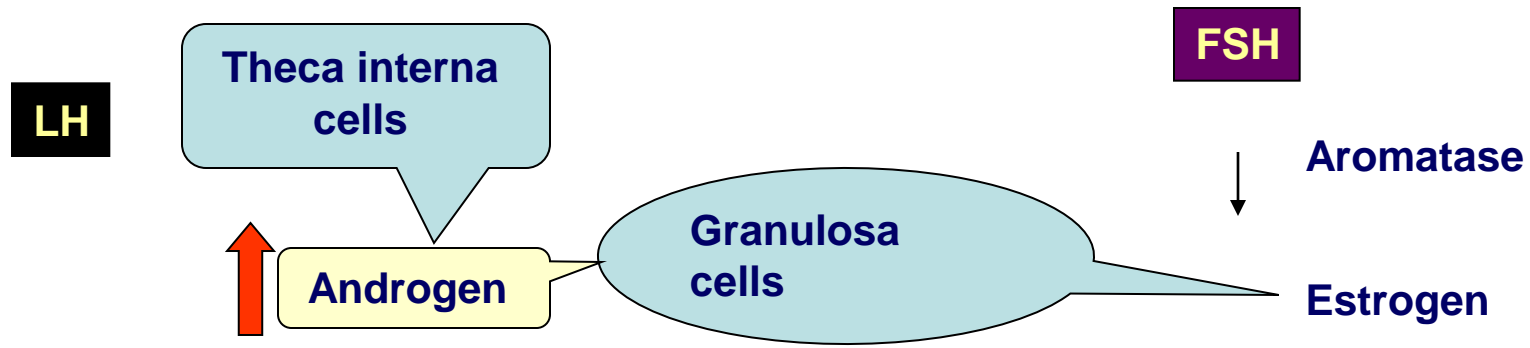
Hormonal regulation of folliculogenesis







Estrogen synthesis



Summary of follicular events during estrus cycle

- Two or three waves of follicular activity emerge at 0,9, 16 days after ovulation.
- The follicle of a wave undergo a common growth phase for 3 days after emergence .At the end of this phase ,deviation begins.
- Deviation has been proposed to be the eminent event in follicle selection.
- Each follicular wave is stimulated by a surge of FSH when the emerging follicles are 4-mm in cow& 6mm in mare. The FSH levels declining during the common growth phase.
- At the beginning of deviation ,only the more developed largest follicle is able to utilize the low FSH. The smaller follicles have not reached a similar developmental stage.
- A small transient elevation in LH begins before deviation and decreases after deviation .LH receptor increase in granulosa cells of the dominant follicle. The LH Stimulates the production of estrogen.

ovulation

Expulsion of the ovum from the follicle

preovulatory Surge of LH (follicle & oocyte)

LH stimulate PGF

‘ ‘

FSH stimulate plasminogen activator

PGS stimulate collagenase

Oxytocin stimulate contraction of SMF. Of theca externa.

1-The ovulatory surge in LH is responsible for:

A-releasing MIF by which the primary oocyte of the GF resumes and completes its first meiotic division, resulting in the formation of two daughter cells, the secondary oocyte and the polar body. The newly formed secondary oocyte enters the second meiotic division and is arrested in metaphase.

B-Initiating acute changes in increasing local prostaglandins, lipoxins ,kinins, splatelet-activating factor cause dilatation of the capillaries in the theca interna of the follicle wall &hyperemic response)

2-Granulosa cells continue to synthesize proteoglcans and hyaluronic acid which attract water thus causing increase in the size of the GF and loosening of granulosa layer (cummlus expansion).

3-just before ovulation, the surface of the ovary looses its blood supply. (stigma) .The connective tissue at the stigma degenerate, loses its strength and rupture by the intra-follicular pressure.

Cumulus expansion :

The preovulatory surge of gonadotrophins induces marked changes in both the follicle and the oocyte – cumulus complex . Oocytes resume meiosis and progress to metaphase II before ovulation.

As oocytes mature in response to the preovulatory gonadotropin surge, cumulus cells secrete hyaluronic acid which becomes hydrated and the spaces between cumulus become enlarged and the cells become embedded in a sticky, mucified matrix (cumulus expansion and mucification)

Thus cumulus expansion is one of several important processes that must occur in preovulatory follicles to enable ovulation .

Types of ovulation

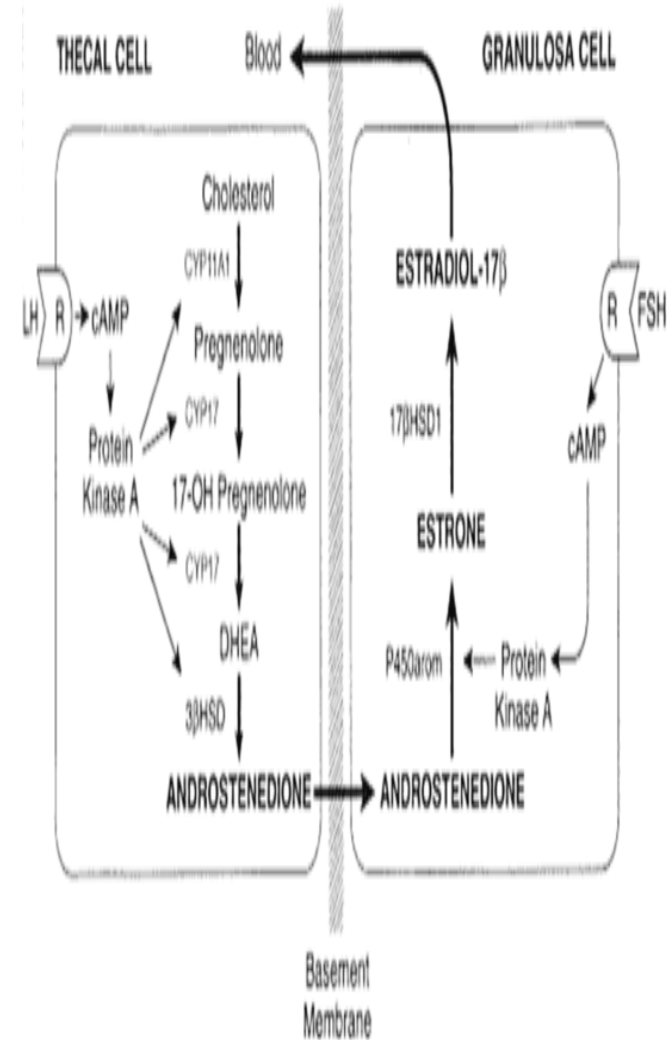
Induced or reflex ovulatory animals : this type is stimulated by the act of copulation .physical stimulation of the cervix triggers the release of gonadotropins from the pituitary. These gonadotropins signals the egg to resume meiosis and initiate ovulation after 30hours from LH surge (she-camel)&10¹/₂ in rabbits.

Spontaneous ovulatory animals : a periodic ovulation pattern independent on mating , in which female ovulates at specific time of the year

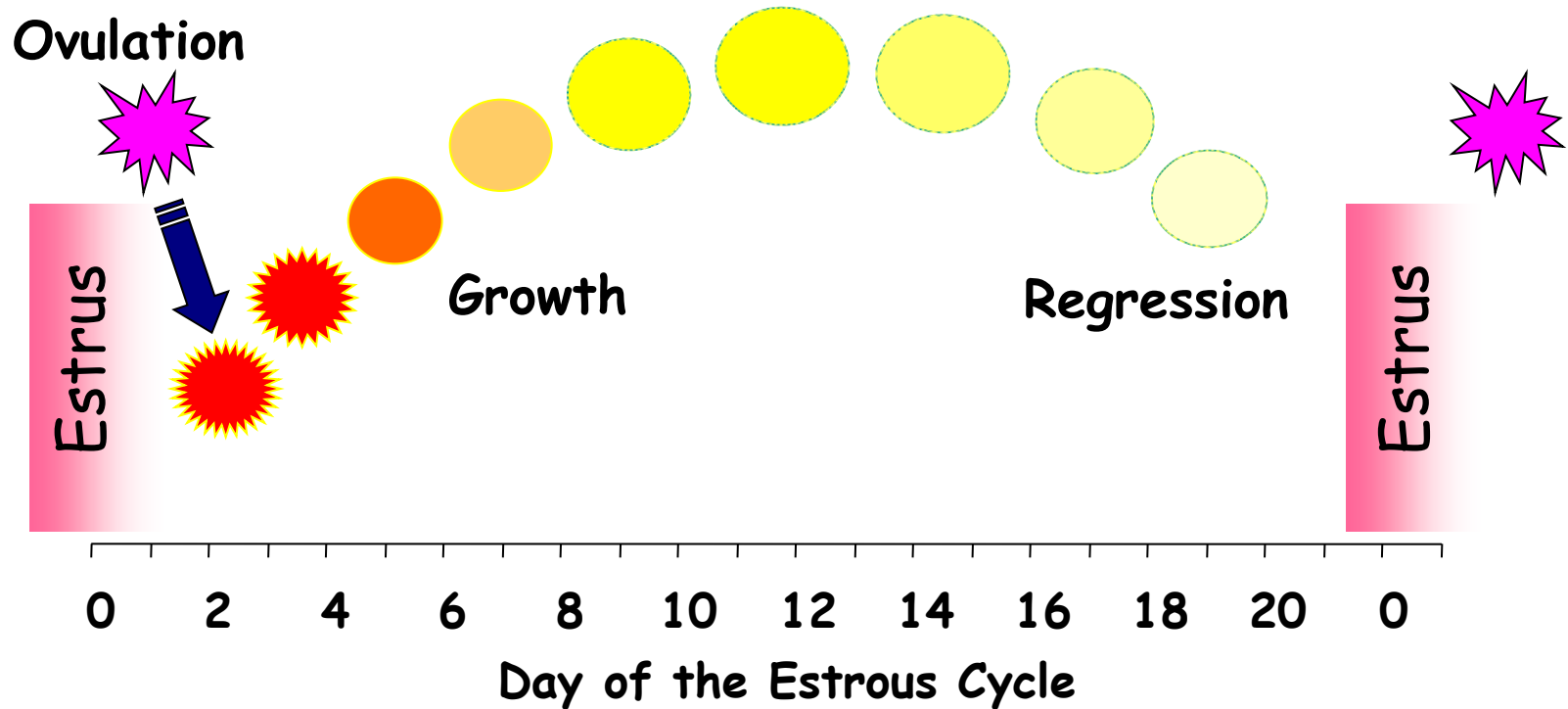
Luteinization

Formation of CL under the effect of LH after the rupture of the follicle & release of oocyte

- **granulosa cells** are transformed into lutein cells (80%) they produce progesterone and convert androgens produced by the theca-lutein cells into estrogen.
- theca – lutein cells (20%)** produce progesterone ,some estrogen and androgens .

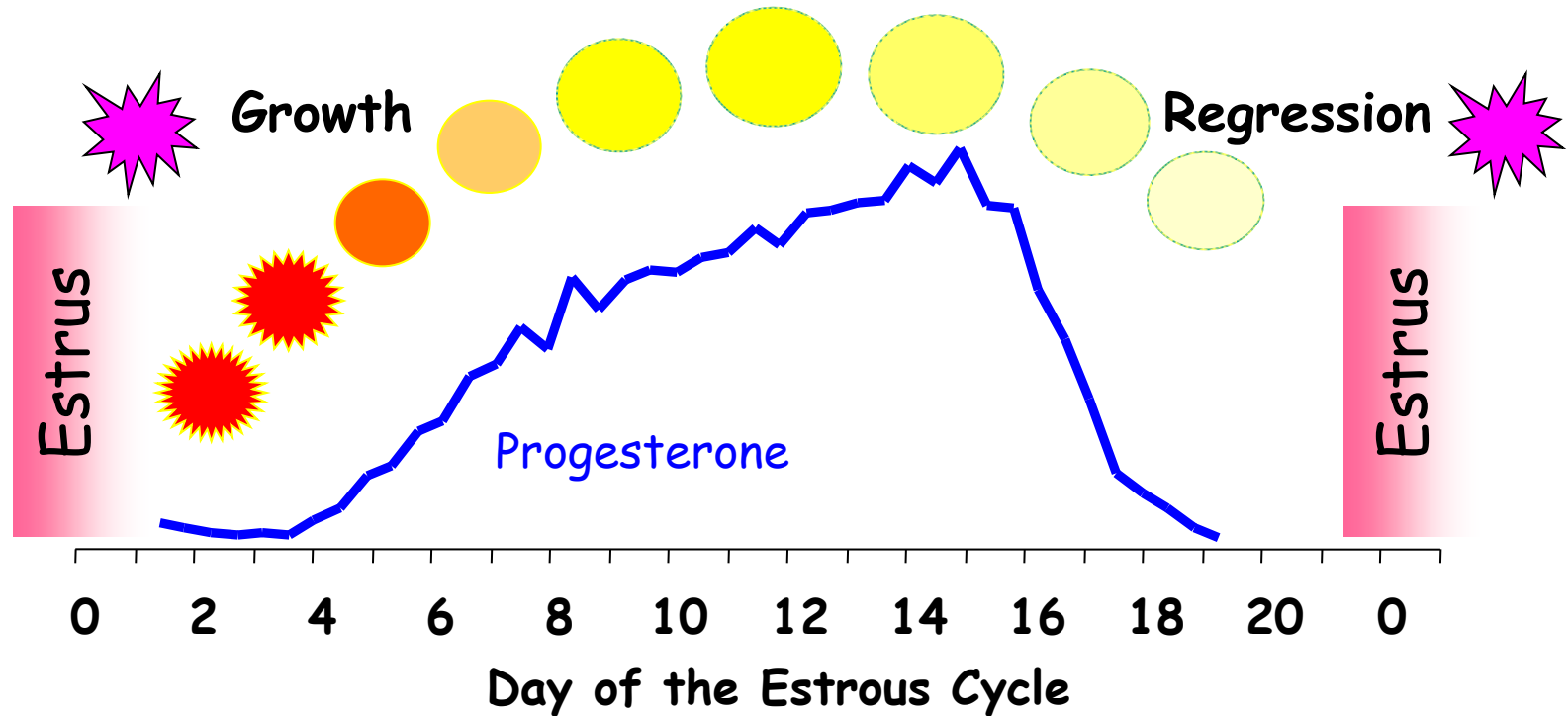


Corpus Luteum (CL) Growth and Regression



- Corpus luteum develops from the ovulated follicle and takes approximately 10 days to reach mature size

Corpus Luteum (CL) Progesterone



- Corpus luteum produces progesterone
- Progesterone is responsible for maintenance of pregnancy after conception occurs

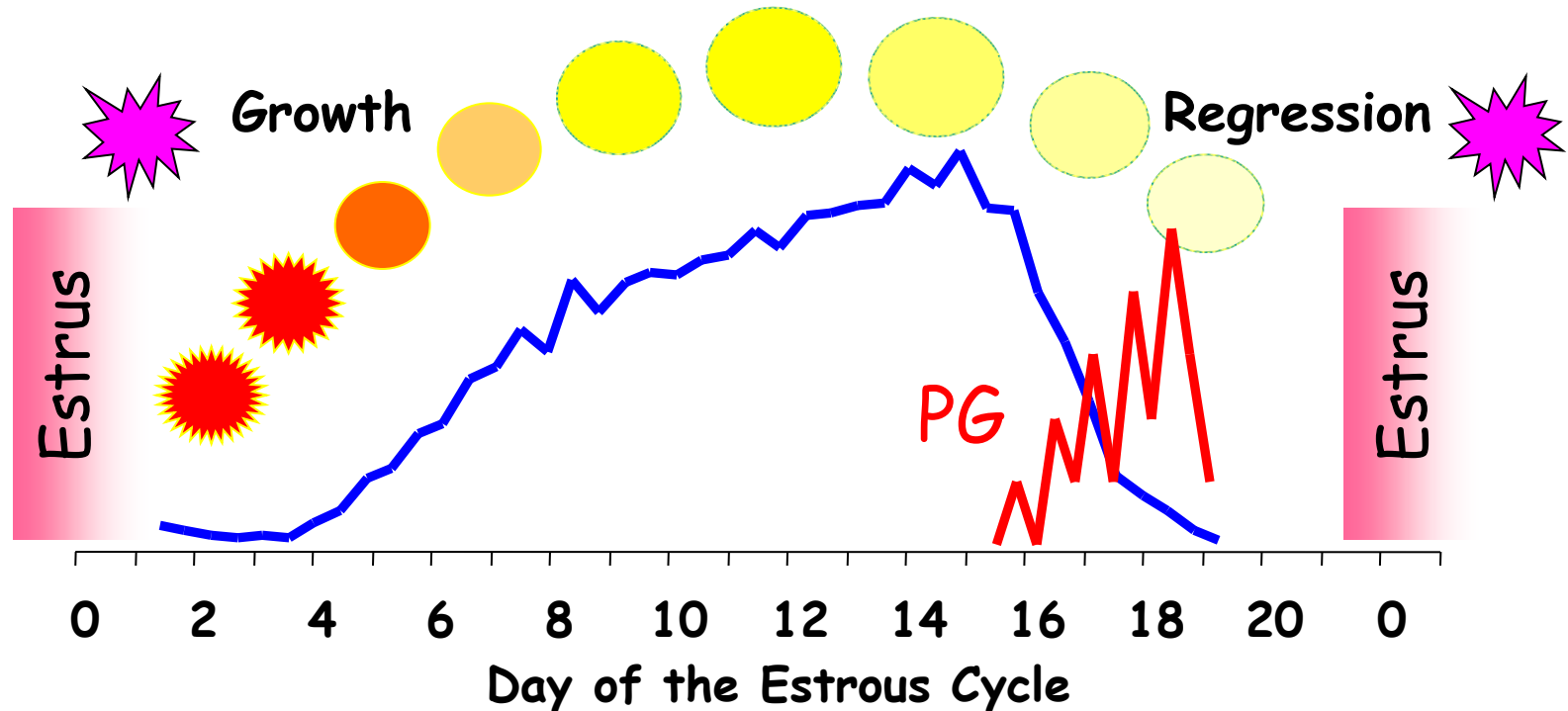
In **rodents** there is blood clot formed in the center which is surrounded by lutein cells forming **corpus haemorrhagicum**. This clot is absorbed and CL become fully developed CL to secrete large amount of progesterone and small amount of estrogen

LH interact with receptors (theca interna) to stimulate the secretion of progesterone and initiate morphological and functional changes.

Luteolysis

Regression of CL and becomes fibrotic and stop to function and a new cycle begins as a result of fertilization failure. The fibrous connective tissue that forms in place of CL is known as corpus **albicans** which persists for sometime before reabsorbed.

Corpus Luteum (CL) Regression Prostaglandin F_{2α} (PG)

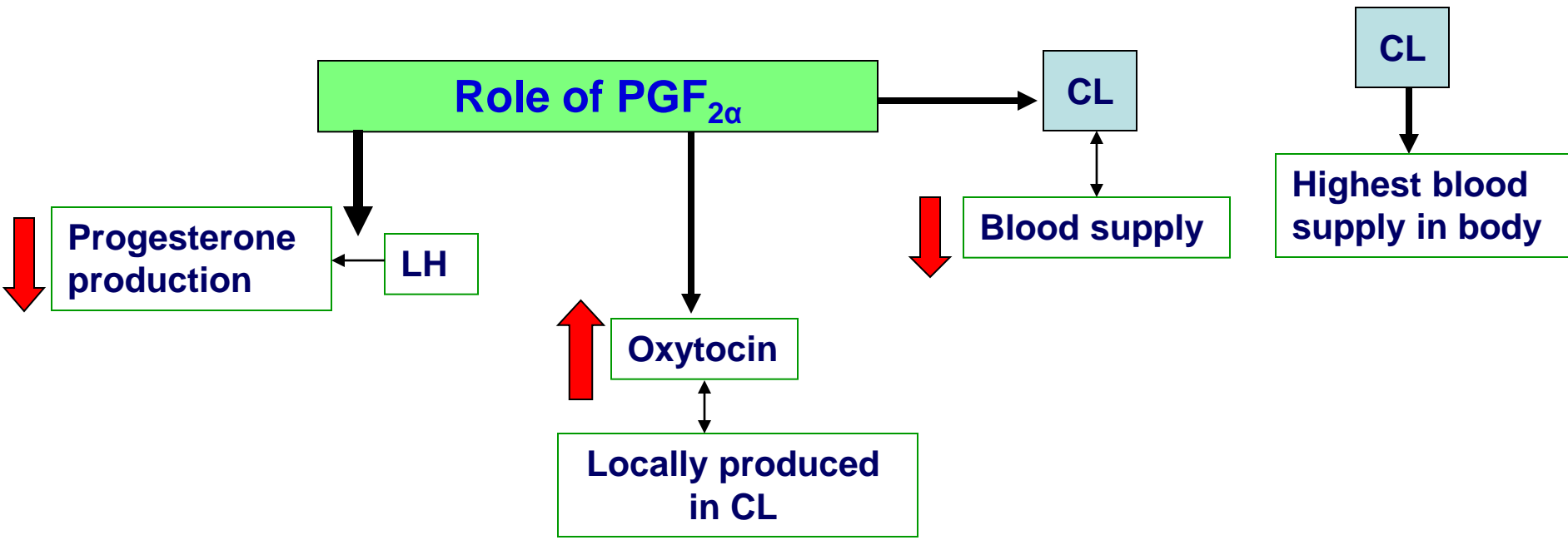


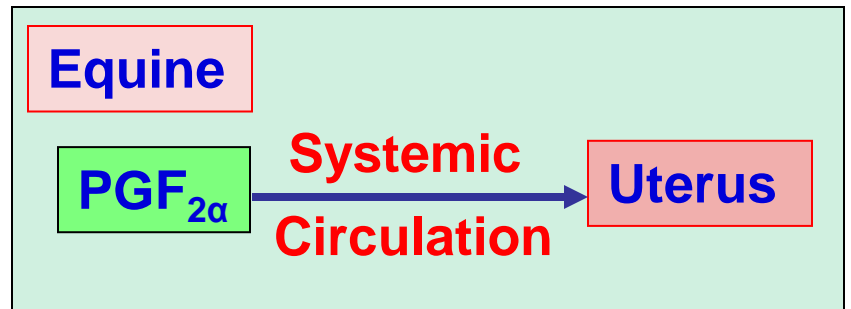
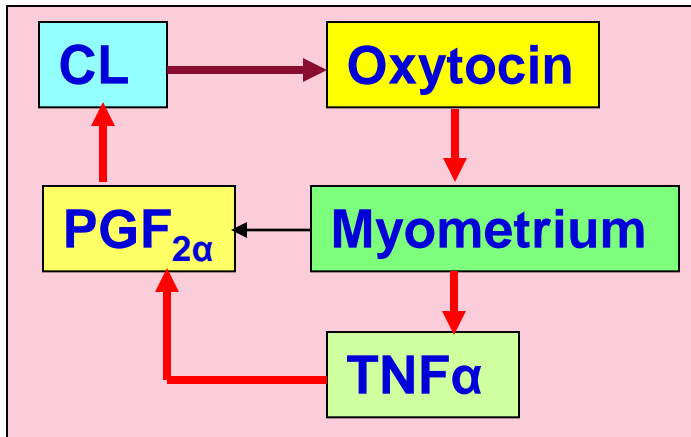
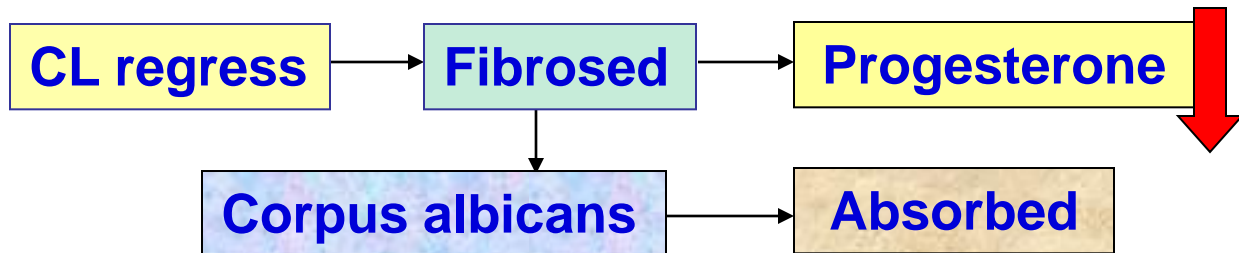
- ❑ Late in the estrous cycle, uterus produces PG which causes regression of corpus luteum
- ❑ PG is the same or similar hormone in "Lutalyse[®]", "Estrumate[®]", "ProstaMate[®]", and "In Synch[®]"

If fertilization and implantation do not occur, the rising level of progesterone and estrogen from CL inhibit GnRH leading to inhibition of LH. So CL degenerates and becomes corpus albicans.

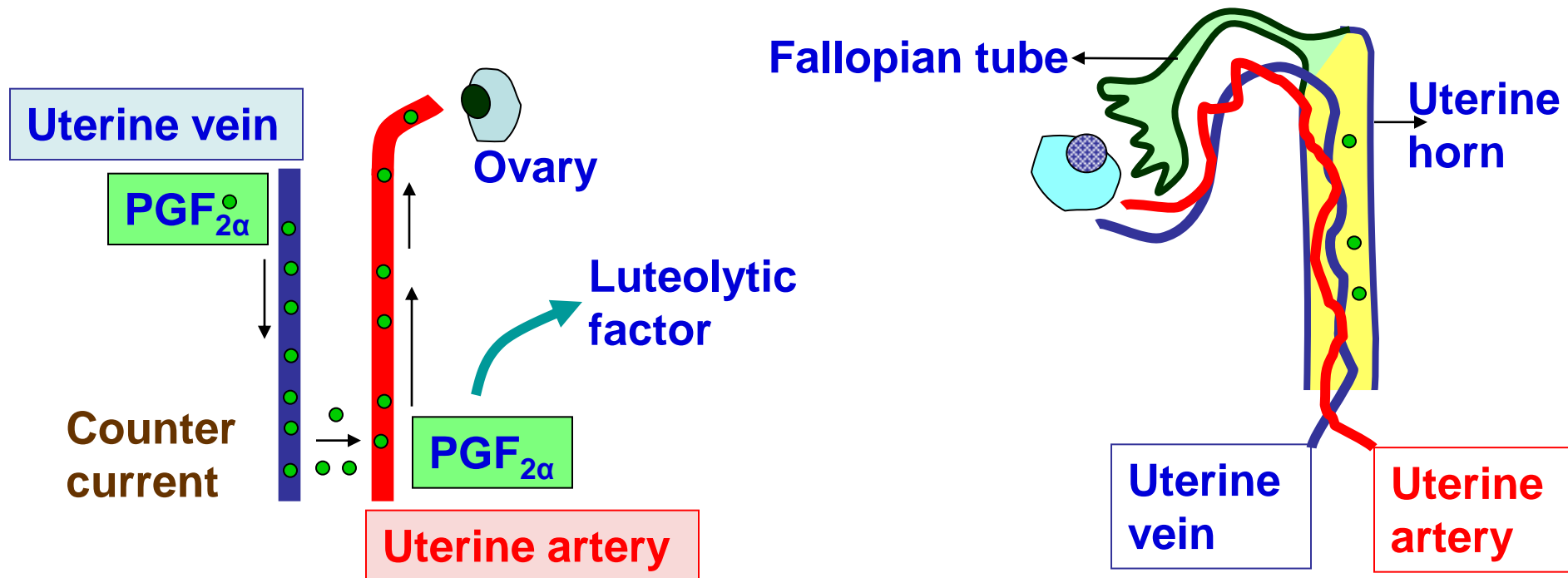
Oxytocin (formed by CL has dual effect):

1. It support secretion of progesterone (lutotrophic) through formation of 3BHSO enzyme(hydroxysteroid dehydrogenase) which help P4 production which in turn leads to formation of PGE enzyme (peptidylglycin- α -amidating mono- oxygenase) responsible for processing oxytocin
2. It increase PGF 2α (from uterus) which lead to Luteolysis.





Local utero-ovarian pathway of $\text{PGF}_2\alpha$ is the mechanism of CL regression in cow & ewe while in mare there is no direct unilateral effect of the $\text{PGF}_2\alpha$ from the uterus to the ovaries, since the uterine artery is relatively straight and caudal to the ovarian vein. Thus, in mares the regression of CL is systemic pathway.



Mode of action of PGF2 on Luteolysis

- Constricting utero –ovarian vessels causing ischemia and starvation of luteal cells.
- Interfering directly with progesterone synthesis by interfering with ability of LH to activate adenylcyclase.
- Competing with LH for receptor site .
- Destroying LH receptor site.

Luteal phase: CL grow under the effect of LH leading to production of progesterone

The uterus become flabby as progesterone decreases its water contents

Increase secretory activity of endometrial glands

The glands appear tortuous ,coiled and become secretory.

Oestrous cycle

Rhythmic sexual behavior patterns develop in female animals after puberty.

Types of estrous cycle:

According to duration (short- long & very long)

Short: 4-5 days as in rat, ferret and mouse.

Long: 2-3 weeks as in cow ,buffalo, mare, ewe and sow.

Very long: from 3-6 month as in bitch.

According to pattern:

Spontaneous estrous: estrous comes at any time of the year (cow-buffalo and mare).

Seasonal polyestrous: estrous appears several times only during season (ewe & mare).

Seasonal monoestrous: one estrous cycle occur once during definite season of the year as in bitch.

Continuous: estrous is continuous and ovulation takes place after copulation as in case of rabbit, cat ,mink, camel and wolf (induced ovulators).

The mature graffian follicle does not end by ovulation but degenerate followed by development of a new follicle .Thus we get a continuous production of estrogen responsible for estrous.

Phases of estrus cycle:

Proestrous:-

Which is characterized by the following:

Ovarian follicle are growing rapidly under the effect of FSH

Begins at 17-21 days of estrous cycle in cattle.

Increase estrogen secretion by the follicle & decrease progesterone from CL

Increase mucosal layers of the uterus and vagina

Increase uterine vascularity and contractility (edematous & turgid).

Proestrous bleeding in bitch due to effect of estrogen.

Reproductive Cycle

Estrus cycle

Menstrual cycle

Heat or estrus

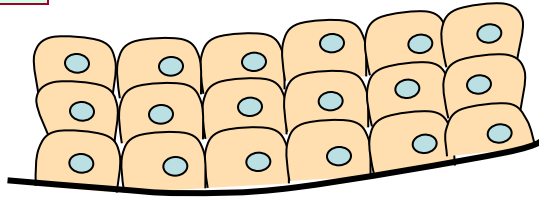
Menstruation

Prominent event

Phases of estrus cycle

Proestrus

Primates



FSH

LH

Estrogen

Mucosal layers

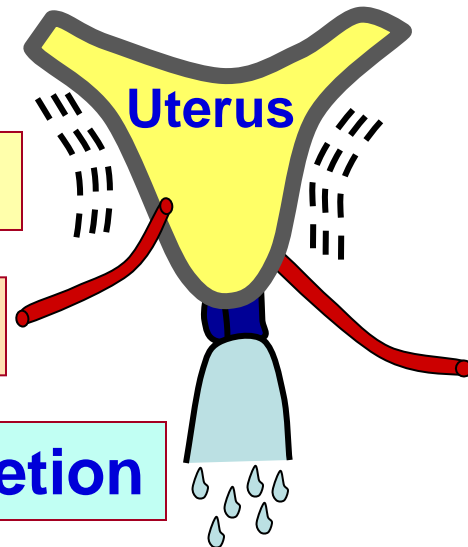
Uterus & vagina

Rapid growth the of the ovarian follicle(s)

Contractility

Vascularity

Serous secretion



Begins day 17-21 of the previous cycle

Estrous:-

Begins at day 1 of the estrus cycle.

High level of estrogen (preovulatory surge of LH behavioral estrus).

All animals ovulates during this phase except cattle.

Cervix is edematous & turgid .Opened cervical canal and the secretion is thin, copious and watery , it can be pulled into threads (spinnbarkeit) aids in the movement of spermatozoa
The secretion is alkaline and contains NaCL increases at ovulation (arborization or palm leaf crystals).

Vagina & vulva (cornification & keratinization)

Metestrus-:

:Begins at days 2-4 of the estrus cycle.

Cow ovulates at the beginning of this phase.

Decrease estrogen and increase progesterone

High level of progesterone (inhibit FSH/ LH–

Inhibit uterine contractility –stimulate endometrial

gland to produce uterine milk (progestational

proliferation).progesterone results in thick

&tough secretion and forms a cervical plug during

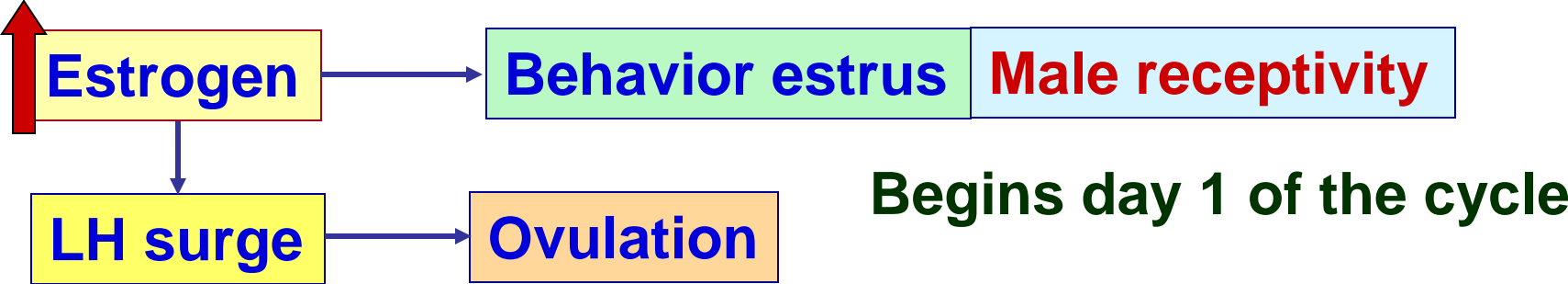
pregnancy closes cervical canal to be impermeable

for spermatozoa penetration.

Estrus

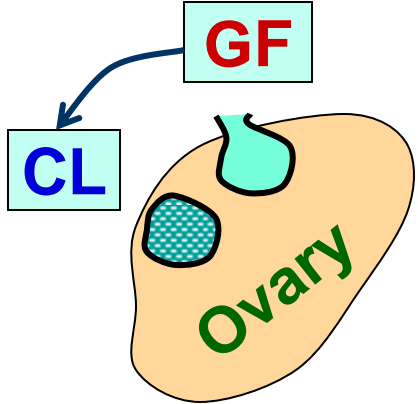
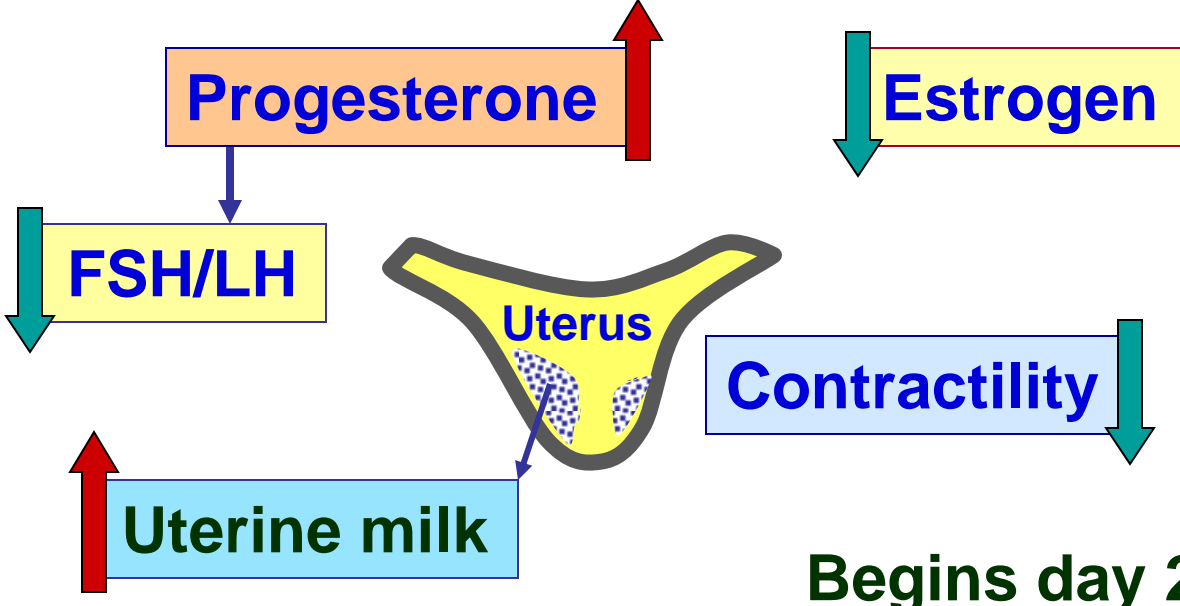
During it:

All animals ovulate **except** cattle



Metestrus

Beginning of luteal activity



Begins day 2-4 of the cycle

Diestrus;

Begins at days 5-16 of the estrus cycle.

Fully developed CL

CL remains functional for about 13 days in ewe and 15-17 days in sow, cow & mare.

If fertilization does not occur ,CL regress at this phase.

Anestrus:

It is a period between the diestrus and proestrus.

Quiescence of the reproductive tract.

Physiological (during pregnancy in spontaneous ovulators-in unmated induced ovulators –in seasonal monoestrus animals)

Pathological: persistence of CL without pregnancy

Diestrus

Begins day 5-16 of the cycle

CL fully Developed

Progesterone

It controls activity of :

Ovary

Uterus

Pituitary

Hypothalamus

CL

Remains active for :

13 days

Ewes

15-17 days

Cow, mare, goat

Anestrus

Physiological

Pathological

Pregnancy

Unmated induced ovulator

Persistence CL

Seasonal polyestrus

Not an estrus phase in polyestrus animals

Some reproductive peculiarities of farm animals

Cow

Length of the estrous cycle (range 18 to 24 days)

Estrus (standing heat)

12 to 18 hours (range 8 to 30 hours)

Ovulation :- Approximately 30 hours after the beginning of standing heat (or 12 to 18 hours after the end of standing heat)

Major structures on the ovary are follicle ... a blister-like structure containing the egg (referred to as oocyte); produces hormone “estrogen”

High amount of estrogen causes “standing heat” and “ovulation” produces hormone “progesterone” that is responsible for maintenance of pregnancy.

Signs of estrus: bellowing-restlessness-clear mucus-homosexual

Ewe :polyestrus- or seasonal polyestrus

**Estrus cycle 17 days- heat 30-40 hours
spontaneous ovulation 8-10 hours before
the end of estrous.**

signs :usually silent using teaser

**Goat: Seasonal polyestrus 20 days heat
30-40 h . Spontaneous ovulation
8-10 h. before the end of heat**

signs : Swollen vulva.

Mare: Some are seasonal polyestrus, others are polyestrus 22 days.

Heat (4-11 days) average 6 days.

Spontaneous ovulation one - two days before the end of heat.

Signs: Swinging of rear quarters towards teaser.

Elevation of tail.

Frequent urination.

Winking of clitoris congested and hyperemic vulva.

Reproductive cycle in she- camel

Seasonal breeders-induced ovulators

No cyclic appearance of CL in non mated females .It is present only in pregnancy.

Follicular wave pattern in she camel(22-24 days):

Follicular recruitment 2-4 days

Growth phase: maximum diameter is 2cm taking 6-10 days

Mature phase:7.6 days.

Regression phase: in absence of mating , mature follicle regress -11.9 days

Bitch: seasonal monoestrus

proestrus: 7-9 days(male & female are interested to each other but coitus is not allowed. Sanguinous discharge due to estrogen

Estrus 4-13 with average of 9 days (the interest between male & female increased and coitus occurs 1-2 days after the onset of heat)-lordosis reflex.

luteal phase 70 days

Spontaneous ovulation continue for 12-72 h.

1-2 days after the onset of heat super fecundation

Queen: Continuous seasonal monoestrous

Cycle (15-21 days)

proestrus : Courtship activities and seeks out male but does not accept him.

Heat (4-9 days)

Rolling

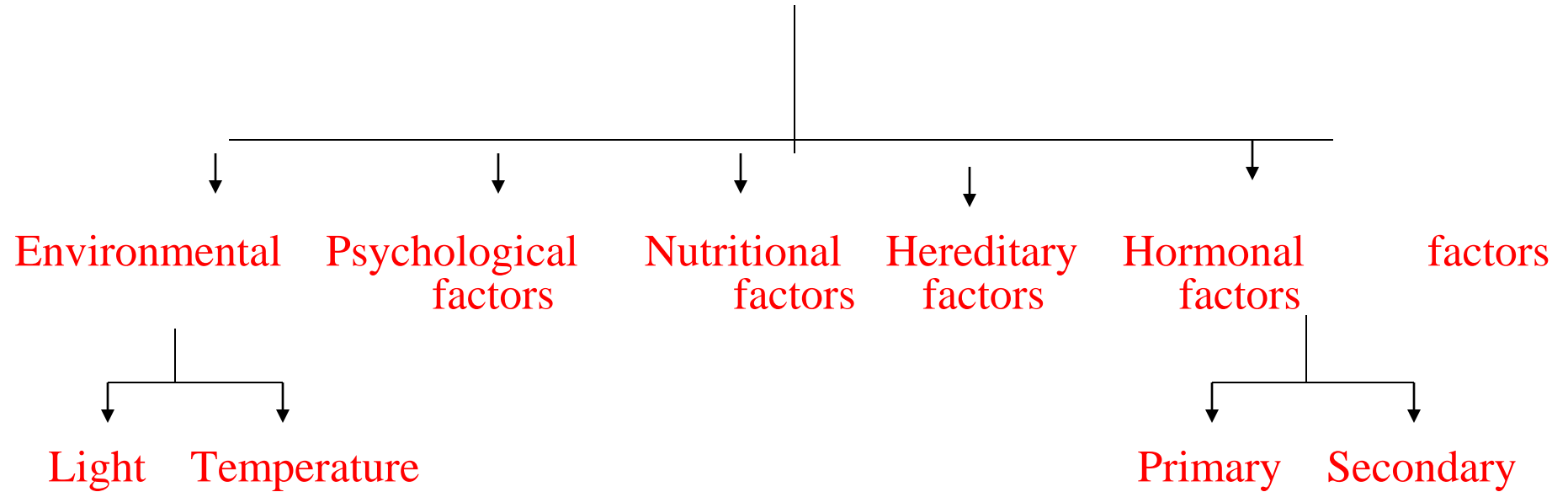
Rubbing against inanimate objects,

Repetitive pawing

Tom (neck biting and mounting)

Ovulation: induced --24-30 h. after coitus superfetation.

Regulation of estrous cycle



A-Environmental factors

I-Light ;

Pineal gland is involved in the timing of seasonal cycle in reproduction (seasonal oestrous cycle) because it secretes photoperiodic hormone which is called **melatonin** which is in relation to daily light-dark cycles in all species , but it only influences the hypothalamic function in seasonal breeder .

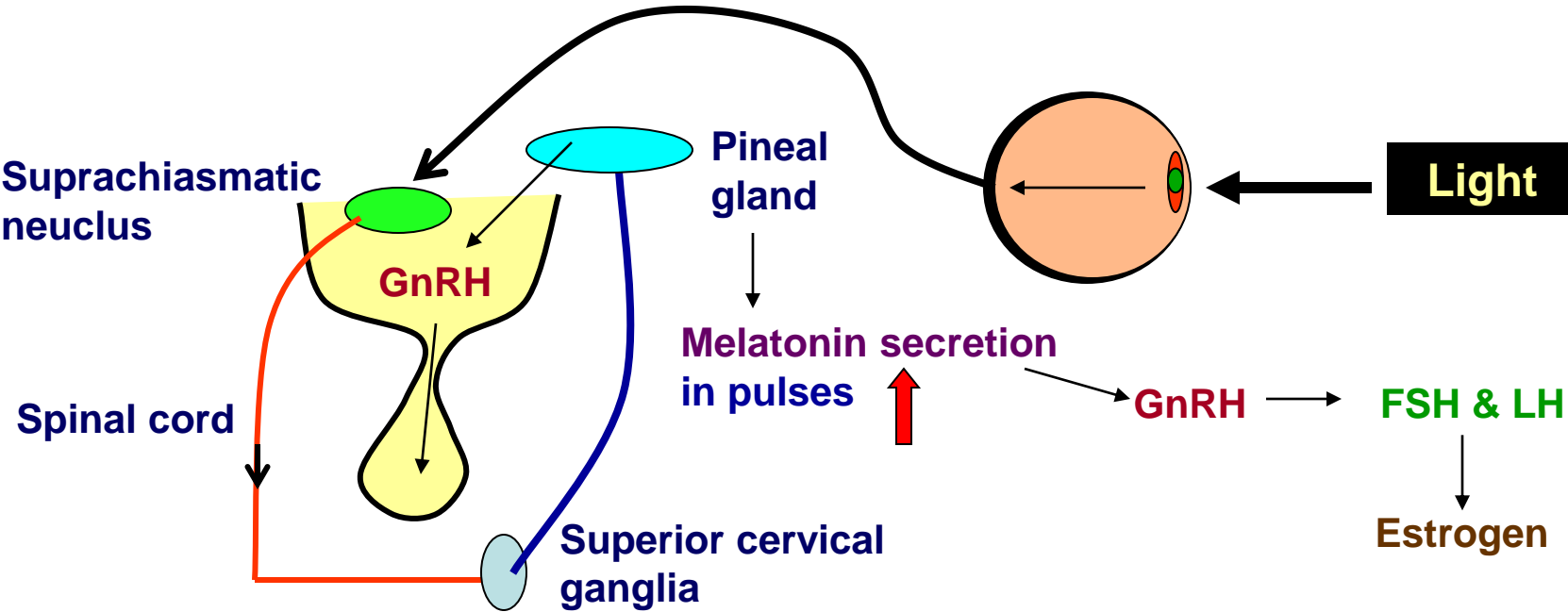
Change in the amount of light falling on the retina of eye produces an action potential that goes to the suprachiasmatic nucleus in hypothalamus.

Then, a descending efferent fiber goes from **suprachiasmatic** nucleus, reach the spinal cord and emerge to the superior cervical ganglia.

Adrenergic post-ganglionic fibers from the superior cervical ganglia supplying the pineal gland stimulate **melatonin** secretion. Melatonin stimulates the hypothalamus to release gonadotropin-releasing factors. The pattern of melatonin pulses during the day is the determining of the melatonin effect.

These releasing factors stimulate pituitary gland to secrete gonadotropin (FSH, LH) which cause the follicle cells to proliferate (folliculogenesis) and secrete estrogen. The **estrogen** has a dual action: enters certain neurons in mid brain and evokes the **pattern mating behavior** characteristic of the species (signs of estrus). Also, estrogen plays important role stimulating the **LH surge** from the pituitary gland, which is essential for the ovulation. However, ovulation occurs 24-45 h after LH surge except in mare in which ovulation occurs before the peak of LH surge.

Effect of melatonin on reproduction



II-Temperature ;

warmth

stimulate the beginning of oestrous cycle.

B-Nutritional Factors ;

Adequate and balanced ration are necessary for regulation of oestrous cycle.

Flushing in sheep may produce super ovulation.

C-Psychological factors ;

In some species , presence of the male stimulates oestrous cycle and ovulation i.e. coitus is considered to exert an accelerating effect on ovulation (e.g., in goat and sow the pheromones secreted from both male and female stimulates oestrous cycle)

D-Endocrinological factors

I-Secondary factors ;

Growth hormone, cortisol, insulin hormone, and thyroxin are necessary for successful reproductive process.

II-Primary factors ;

A- Hypothalamic hormones (GnRH) ;

secreted from the hypothalamus and stored in the median eminence, then they are released in pulses and cause secretion of F.S.H. and L.H.

Hormonal control of ovarian cycle

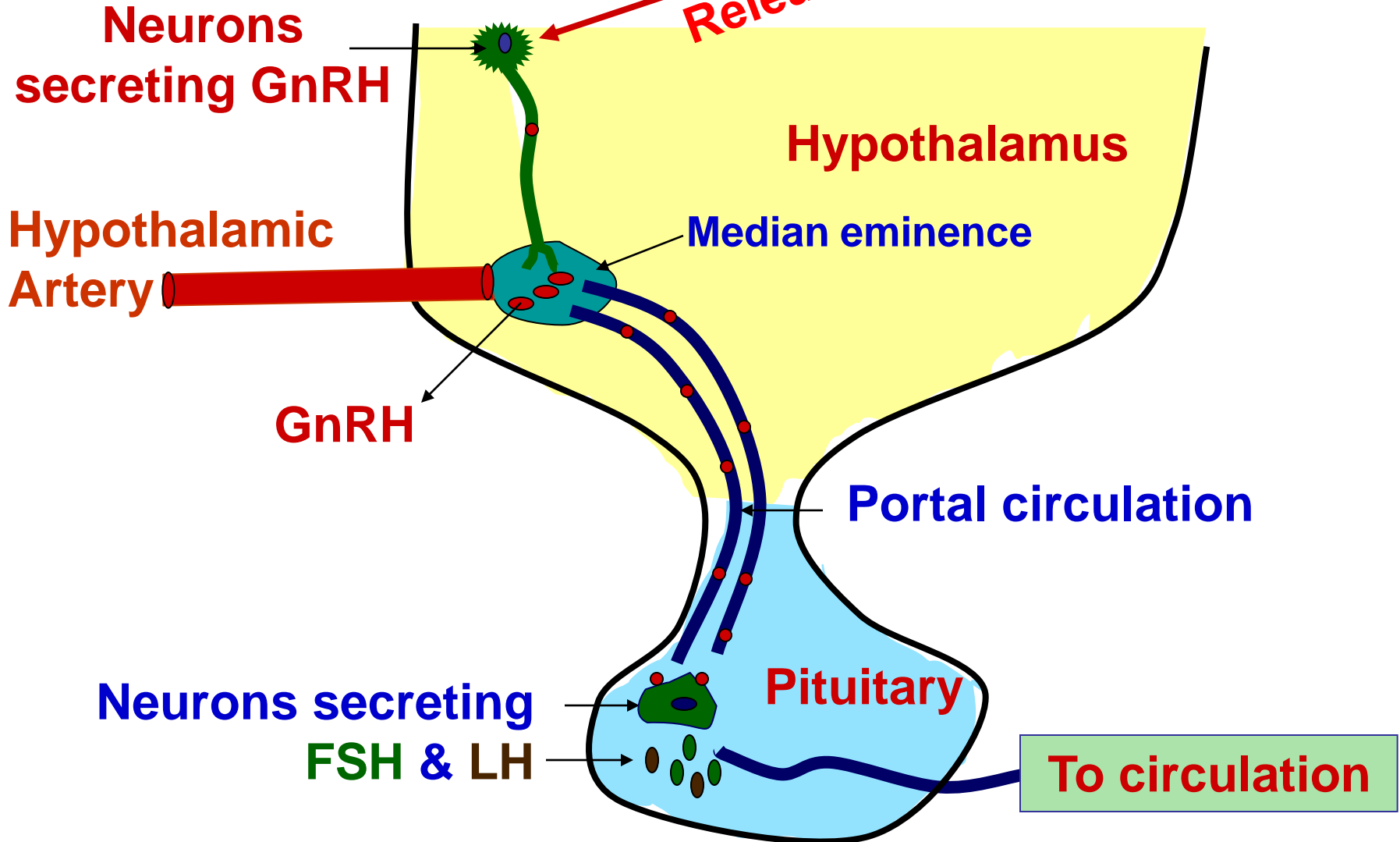
Hypothalamic hormones

Pheromones

Coitus

Rabbit

15minutes
Release



B-Pituitary hormones ;

1 *-Anterior Pituitary hormones* ;

-F.S.H, L.H. and prolactin

FSH & LH act on the ovary and cause follicular ripening and estrogen secretion . The preovulatory surge of L.H. stimulates the granulosa cells to grow and secrete progesterone.

-Post.Pit.Hormones -Oxytocin

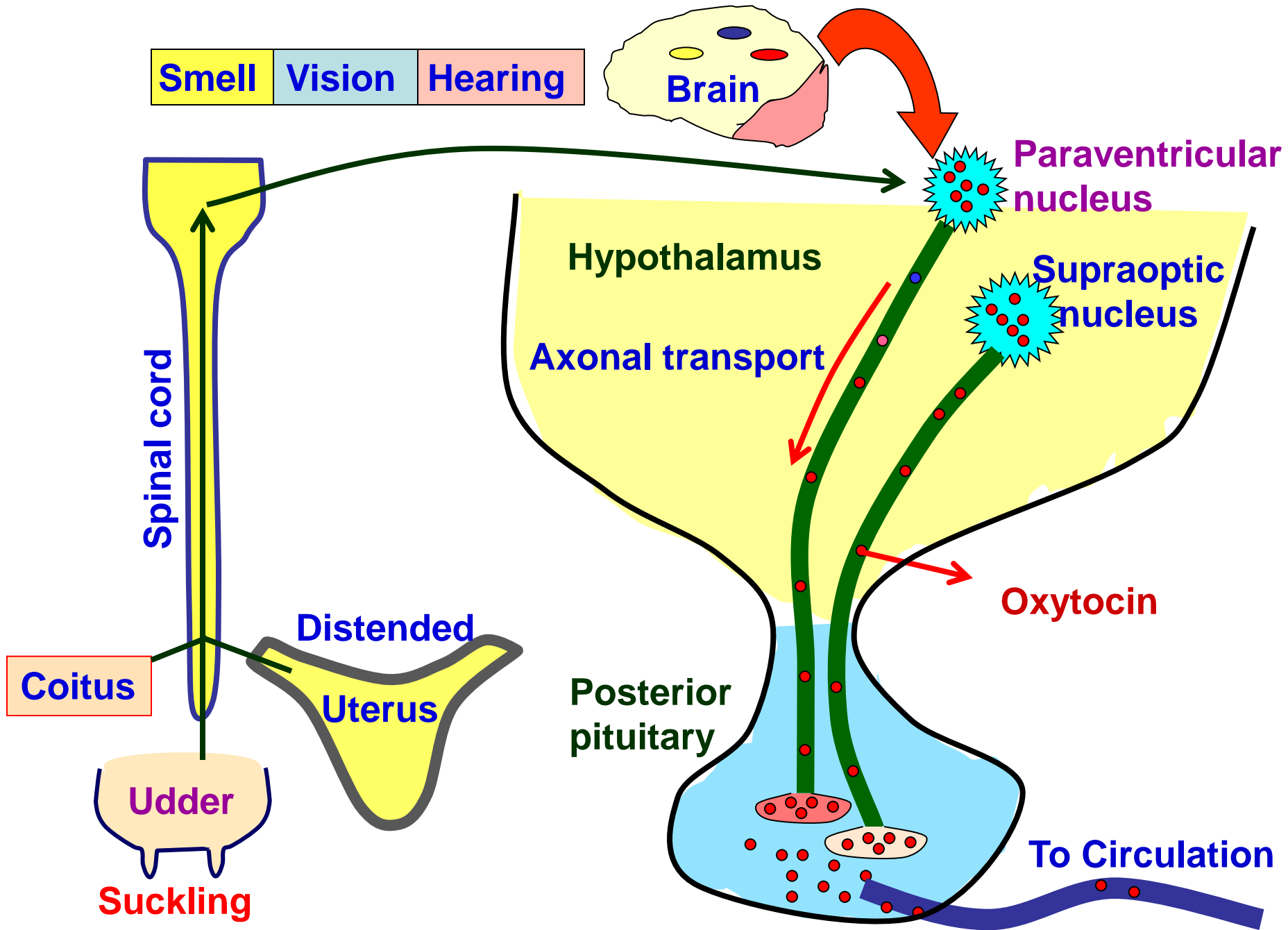
It is synthesized from hypothalamus and transported to post. Pit.(stored).

The hormone is released by increasing nervous activity in the supra-optic and para-ventricular nuclei which is stimulated by:

- 1-Nervous impulses in teat (suckling or milking).
- 2-Genitalia (during copulation & parturition).

Function of oxytocin:

- 1-Contraction of G.Fduring estrous (ovulation)
- 2-Increase oviduct and uterine motility for ascendance of spermatozoa during coitus.
- 3-Causes luteolysis.
- 4-Parturition.
- 5-Let down of milk.
- 6-transport of ova down to the uterus.



C-Female sex hormones:

1- Ovarian hormones (estrogen-progesteron-bradykinin—relaxin—inhibin)

2- Uterine hormone (prostaglandins).


Role of Estrogen

Has DUAL effects;

Very high dose 

 Suppress FSH

-ve feedback

High dose 

 Release of LH

+ve feedback

Role of Progesterone

Suppress FSH & LH

Follicular phase

At the end of luteal phase of previous cycle

 Progesterone

Estrogen

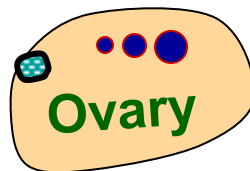
Inhibin

LH 

FSH 

NO CL or GF

Luteolized CL 



GF not selected

Anterior pituitary hormones

FSH

LH receptors on antral follicle



Follicular growth

Synthesis of Inhibin B

Synthesis of estrogen

LH

Synthesis of progesterone

Formation of CL

Synthesis of Inhibin A

Meiosis of oocyte

Follicle selection

Follicle dominance

Ovarian hormones

Inhibin

Ovarian follicle

Primates

Inhibin A

Inhibin B

Ruminants

FSH secretion



Estrogen

sex organs

Uterus

Uterine motility

Oxytocin receptors

Vagina

Vaginal wall thickness
and Vascularity

Glycogen deposition

glycogenolysis

Acidic vagina

Lactic acid

Cervix

Cervical relaxation

watery secretion

Udder

Duct system

Signs of Estrus

Female fat distribution

Broad pelvis

Metabolic rate

Na & H₂O retention

Ca²⁺ deposition in bone

Prolactin release



Progesterone

Progestional block

Blood supply

Myometrial activity

Spiral arteries **Primates**

Quiescent uterus

Uterus

Endometrial thickness

Uterine glands **Secretory activity**

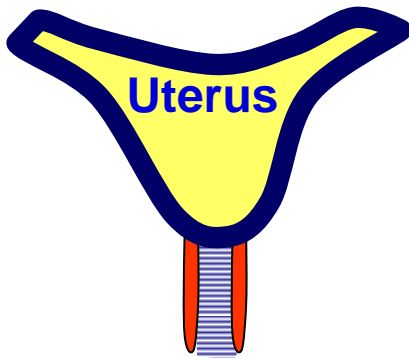
Glandular part of udder

Cervical closure

Thick cervical mucus

Estrogen

body temperature



Bradykinin hormone:

Isolated from follicular fluid and released at the time of ovulation

Activated by fallopian tube secretion results in relaxation of its muscles.

This mechanism creates a negative pressure in the oviduct to trap the released ovum.

Relaxin:

Relaxes pubic symphysis and other pelvic joints and softens and dilates the uterine cervix during pregnancy. Thus it facilitates delivery. It inhibits uterine contraction and plays a role in the development of the mammary gland.

Inhibin:

Higher level of FSH in blood stimulates the granulosa cells to produce inhibin to lower FSH (feedback mechanism).

Prostaglandins

Contraction of:

Follicular wall



Ovulation

luteolysis



**Synchronization
of estrus**

**All animals get in
estrus together**

Uterus

Uterine contraction

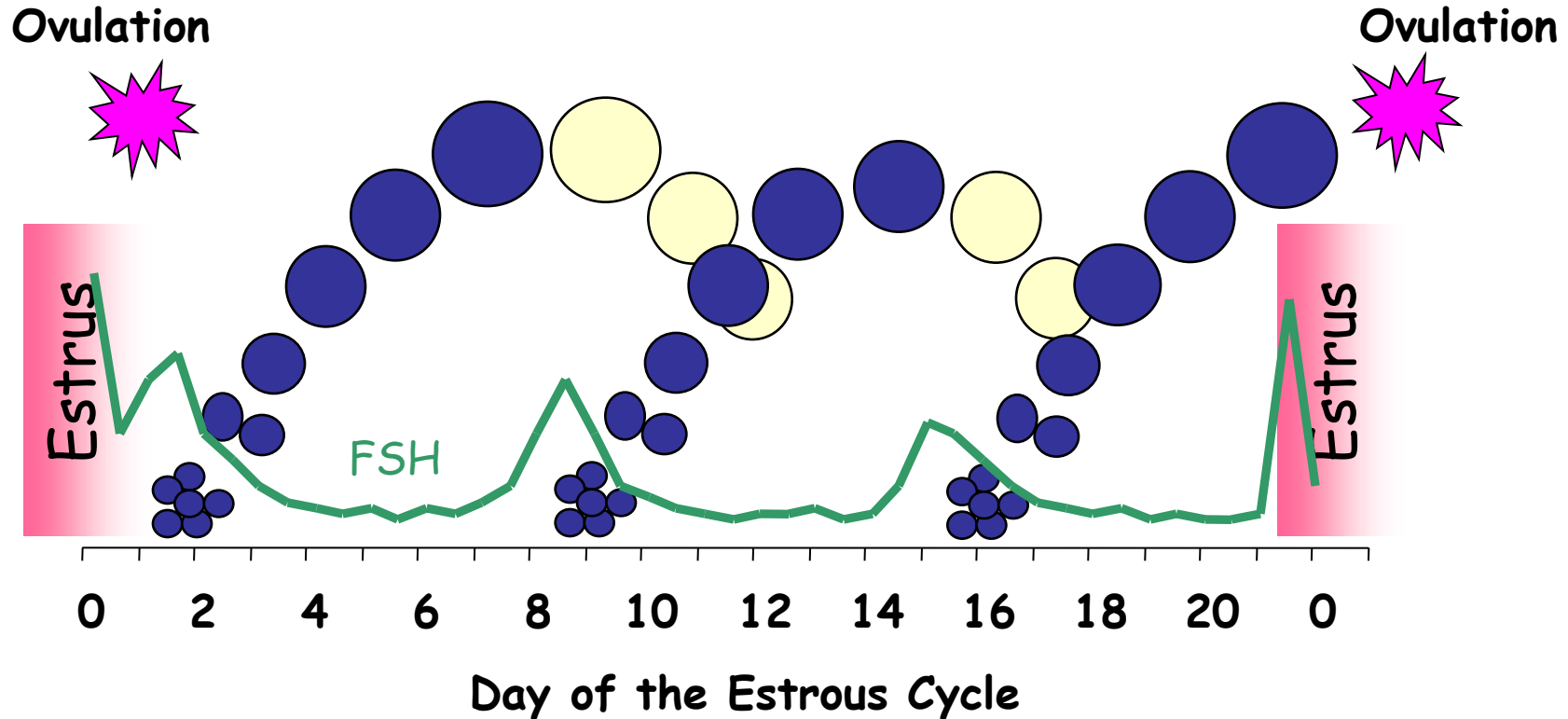
During parturition

Liquefy cervical mucus

Sperm transport

Endocrinology During the Estrous Cycle

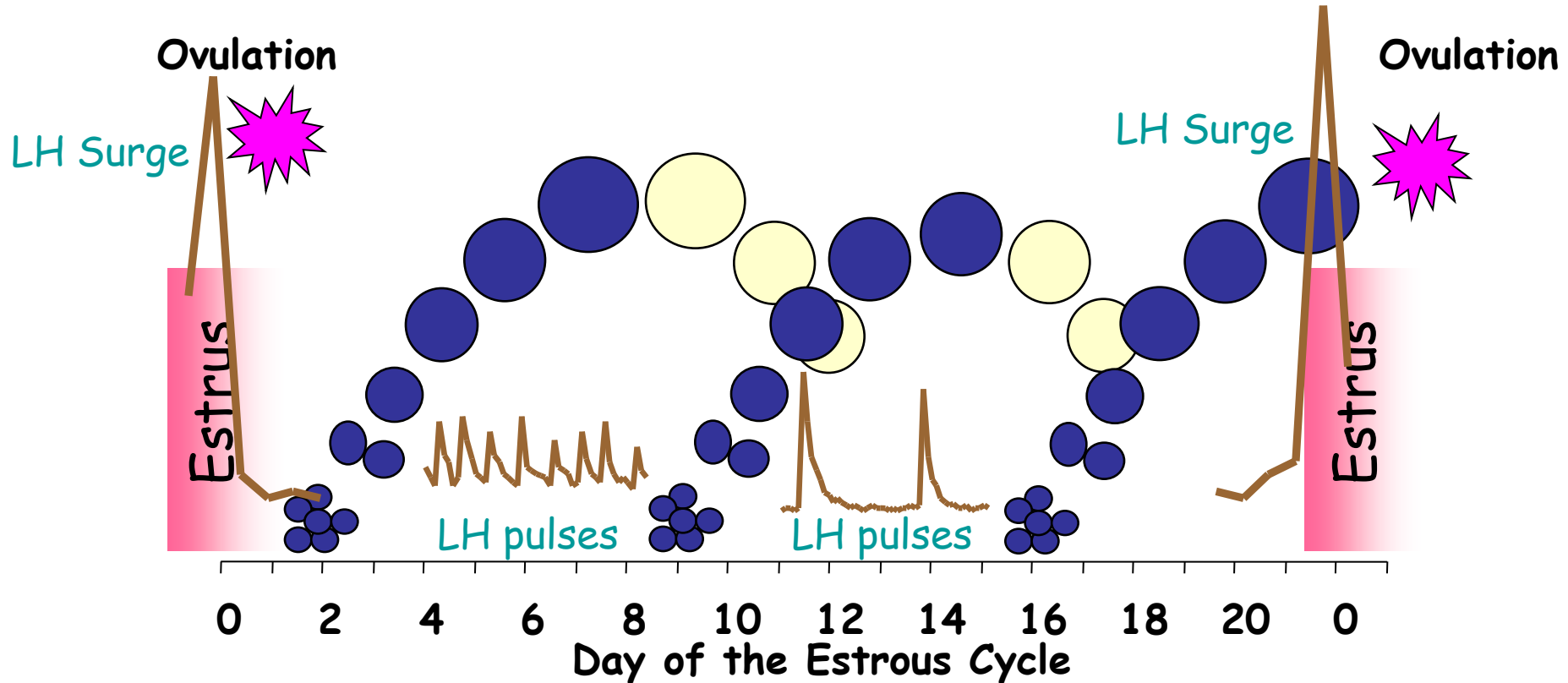
Follicle Stimulating Hormone (FSH)



□ Example shown for cattle having 3 follicular waves during a 21-day estrous cycle

Endocrinology During the Estrous Cycle

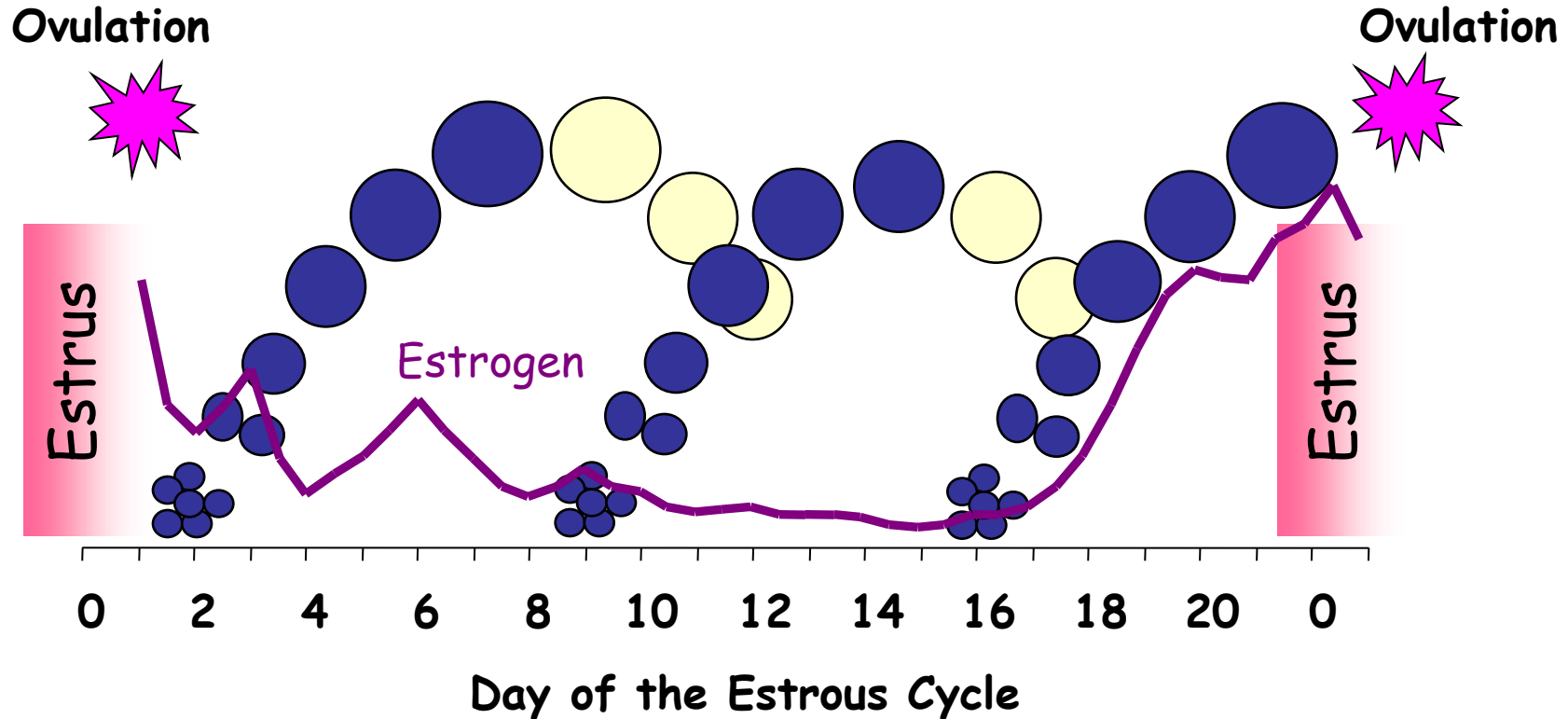
Luteinizing Hormone (LH)



Example shown for cattle having 3 follicular waves during a 21-day estrous cycle

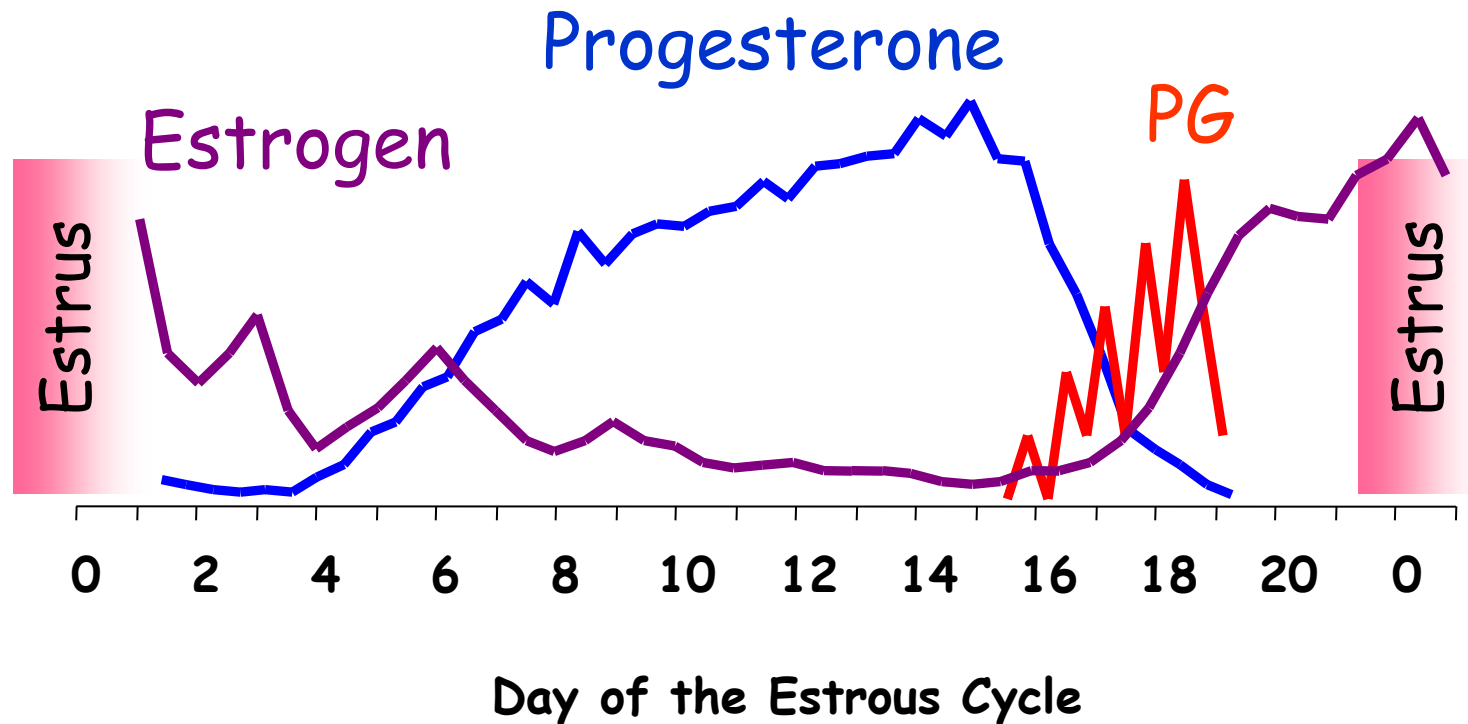
Endocrinology During the Estrous Cycle

Estrogen



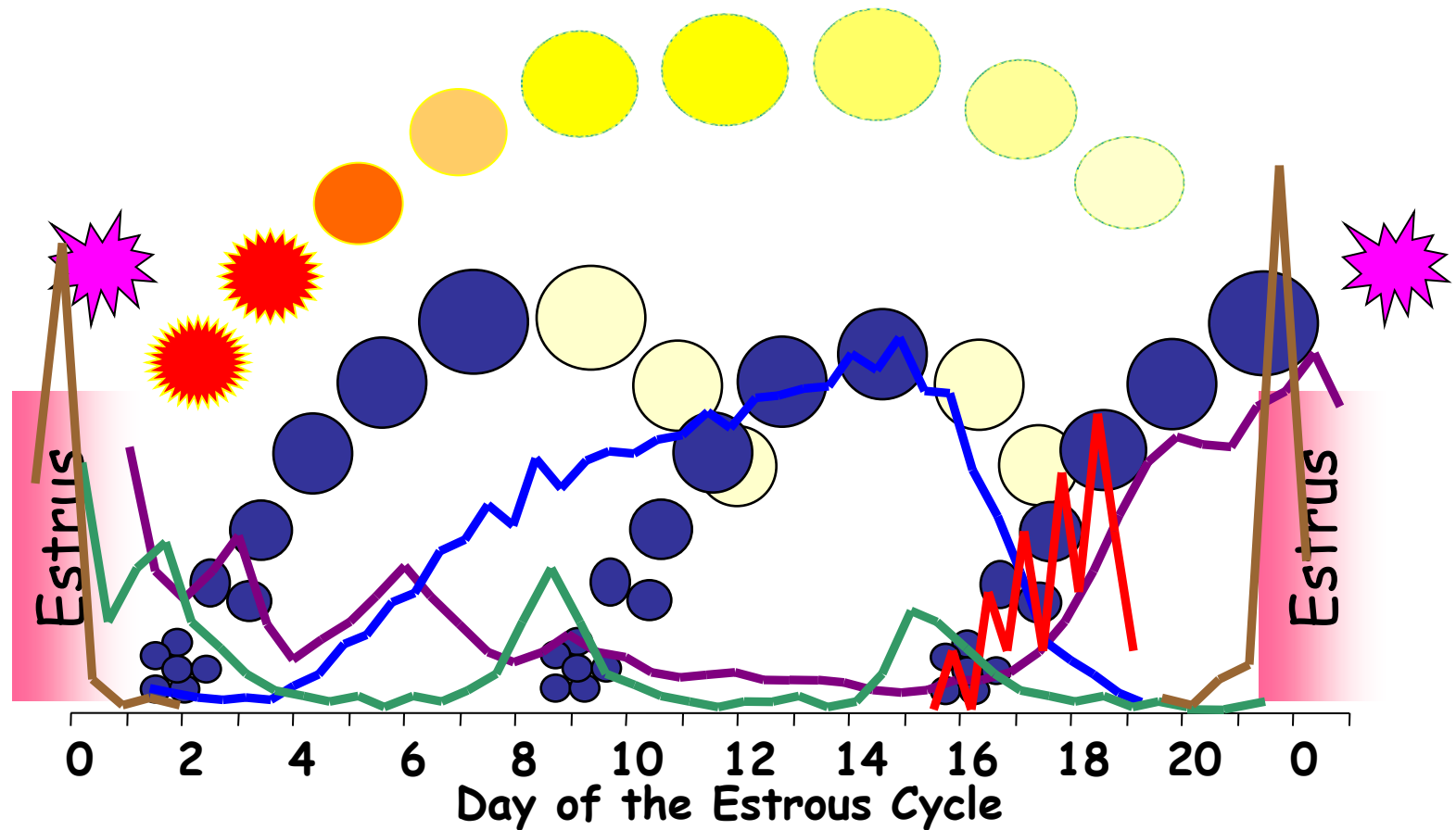
□ Example shown for cattle having 3 follicular waves during a 21-day estrous cycle

Endocrinology of the Estrous Cycle

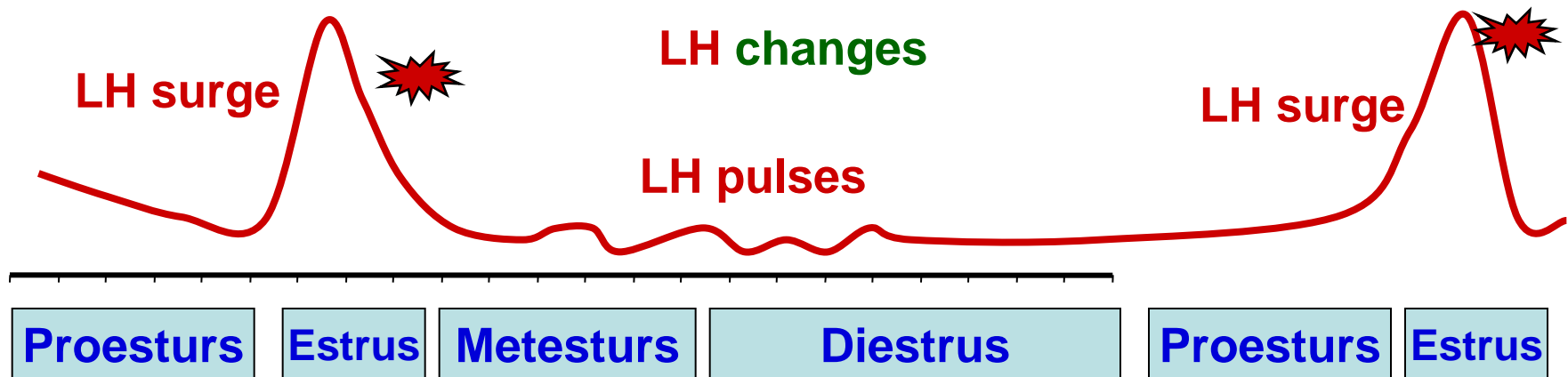
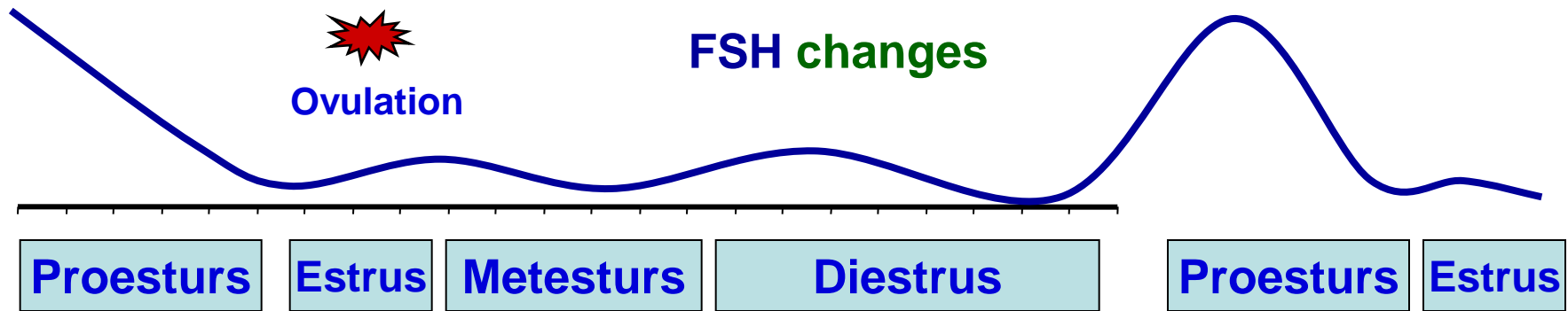
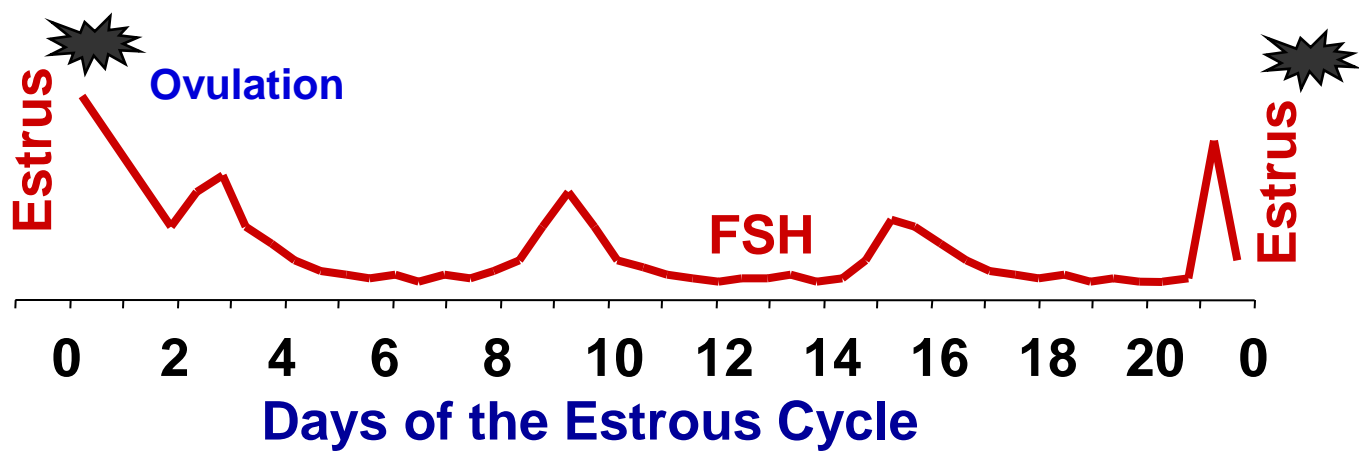


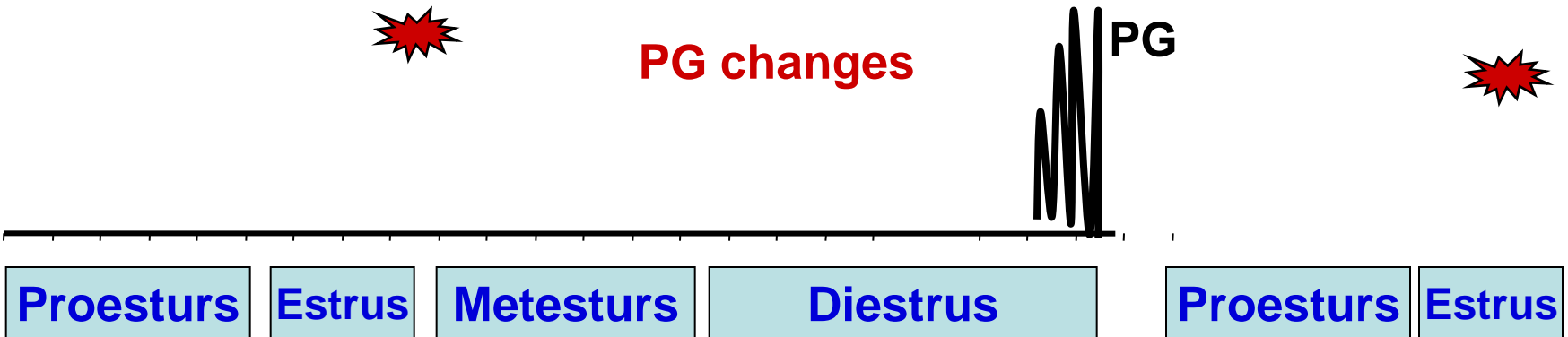
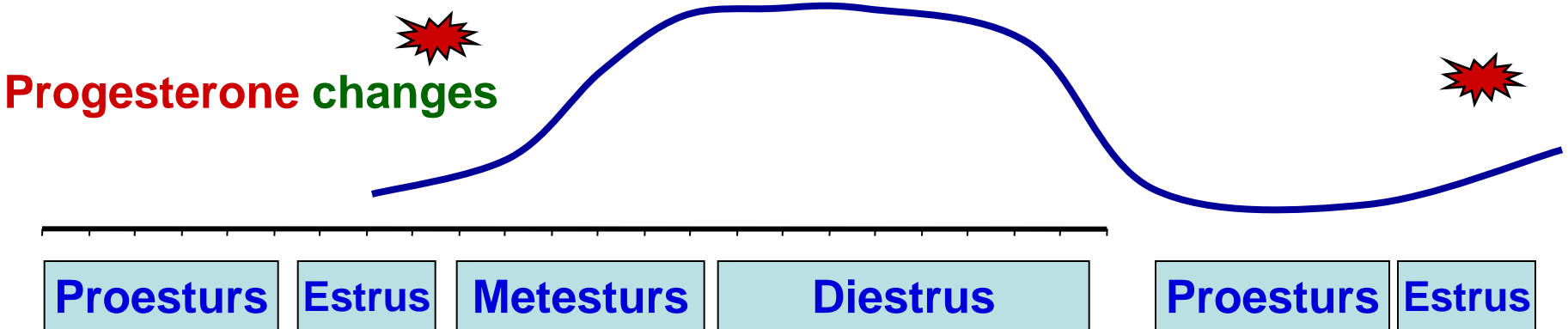
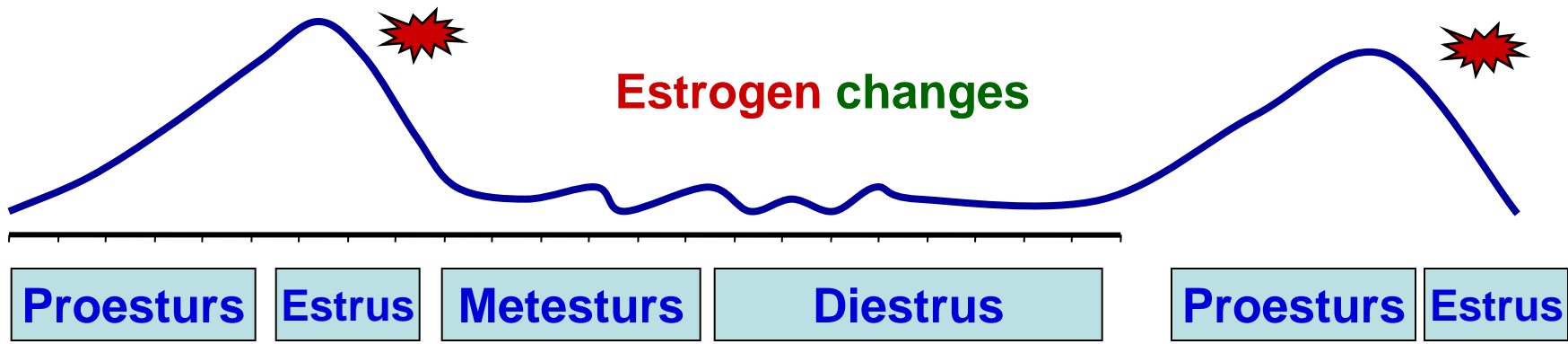
- Relationships among estrogen, progesterone, and PG during the 21-day estrous cycle

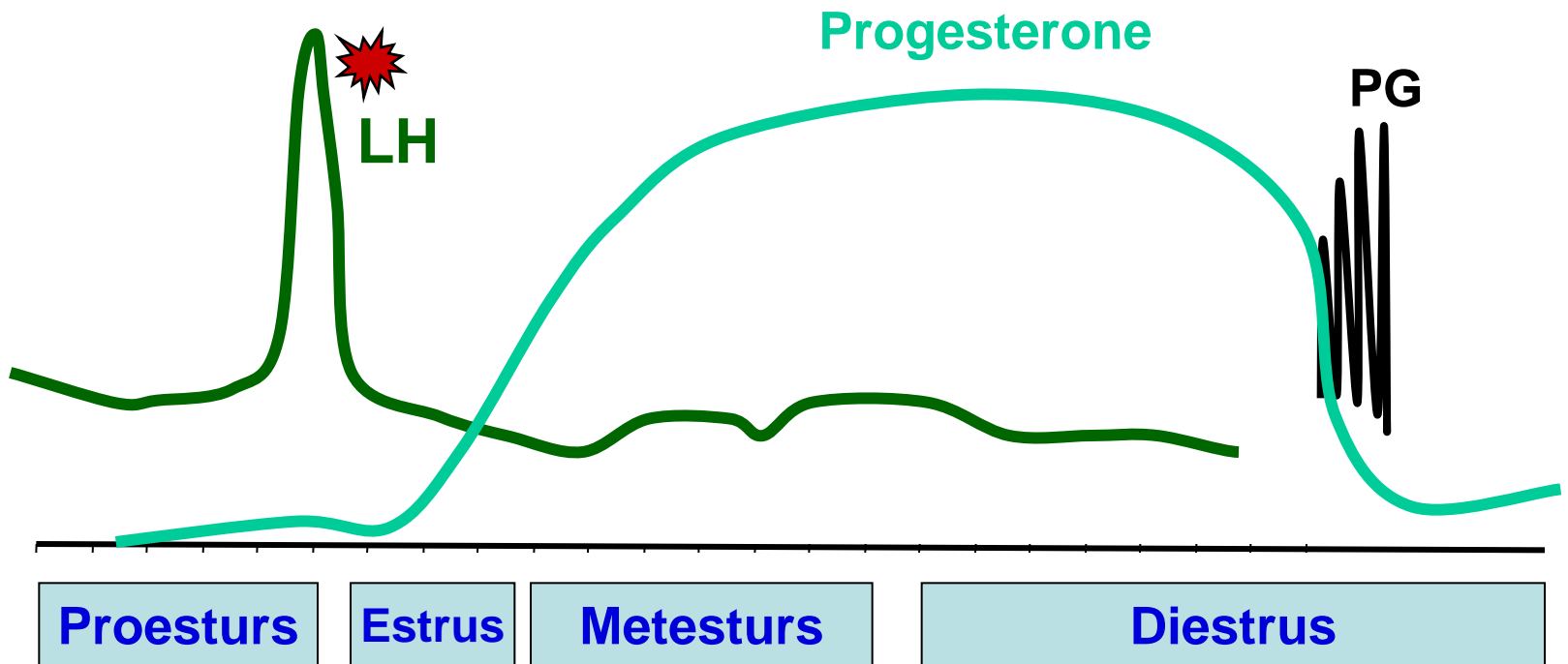
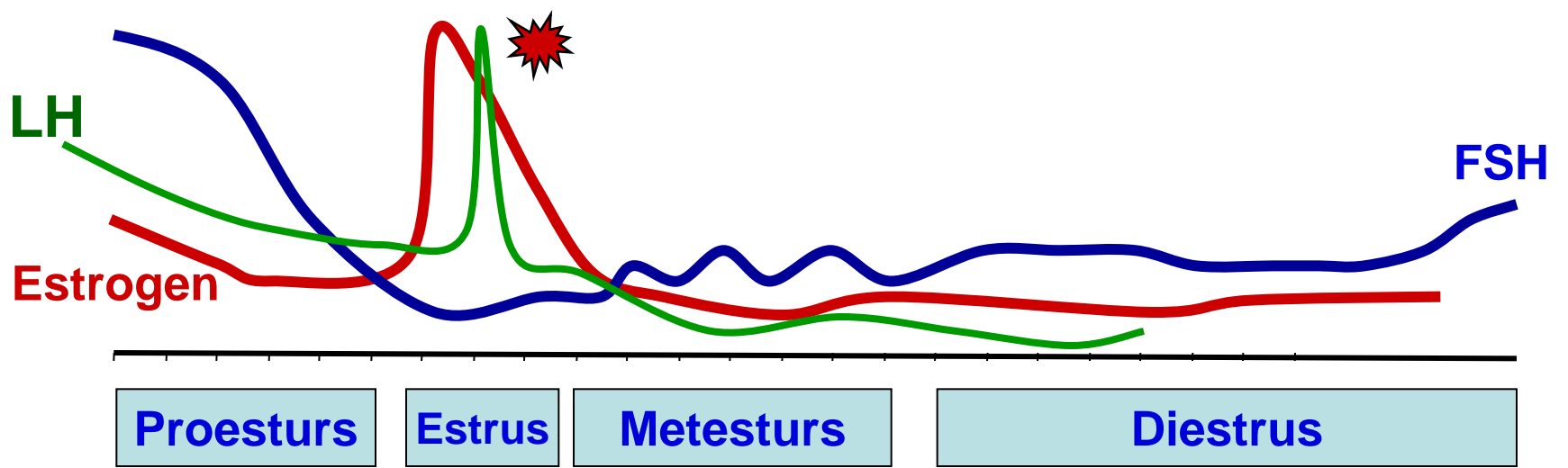
Physiology and Endocrinology of the Estrous Cycle



- Relationships among structural and hormonal changes during the 21-day estrous cycle (example shown for cattle having 3 follicular waves)

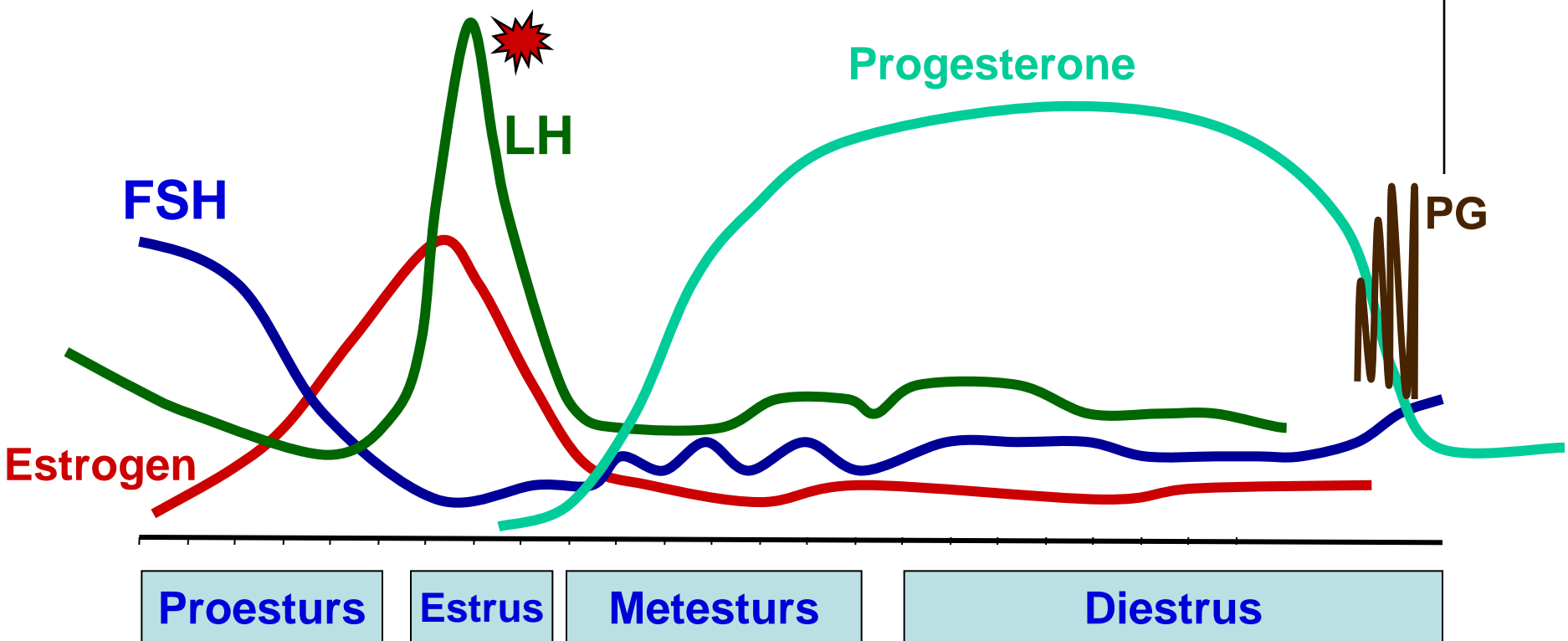






Overall hormonal changes

New cycle ← Luteolysis



Phermones: are substances that are secreted by one sex and when detected by the other sex, it induces activation of its sexual drive.

In some males a special gland is located in the head region near the horns called preputial glands, it secretes volatile substances that can be smelled by the females and increase their sex drive.

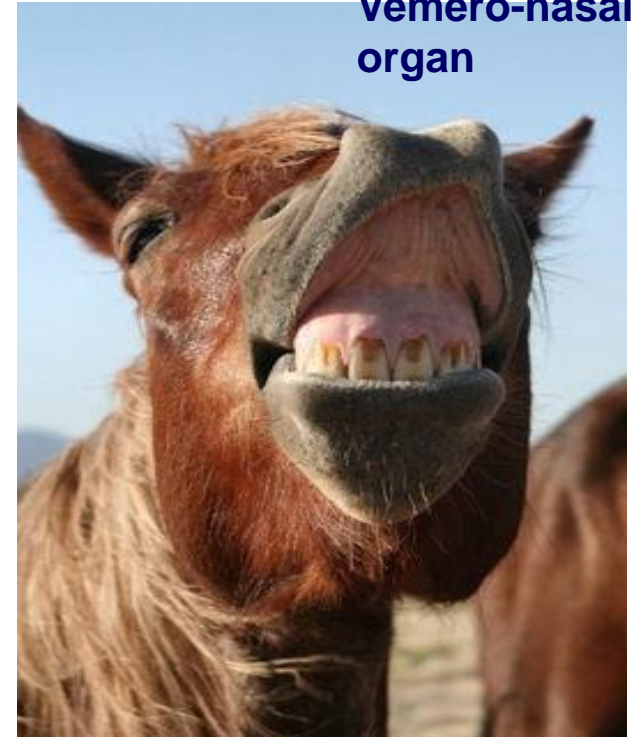
Also the sloughed keratinized epithelium lining the vagina of female during heat period becomes decomposed by the action of normal flora inhabiting the vagina and the result is a wide variety of volatile fatty acids specific for that species.

These volatile fatty acids are a signal for the male to copulate with the female.

In bitch a special substance called methylparahydroxybenzoate is produced specifically to attract male to female.

Pheromones

Flehmen or Lip curling



Vomero-nasal organ

methyl-parahydroxybenzoate

In dogs

Sent glands at anus

Sloughed epith. of vagina at estrus

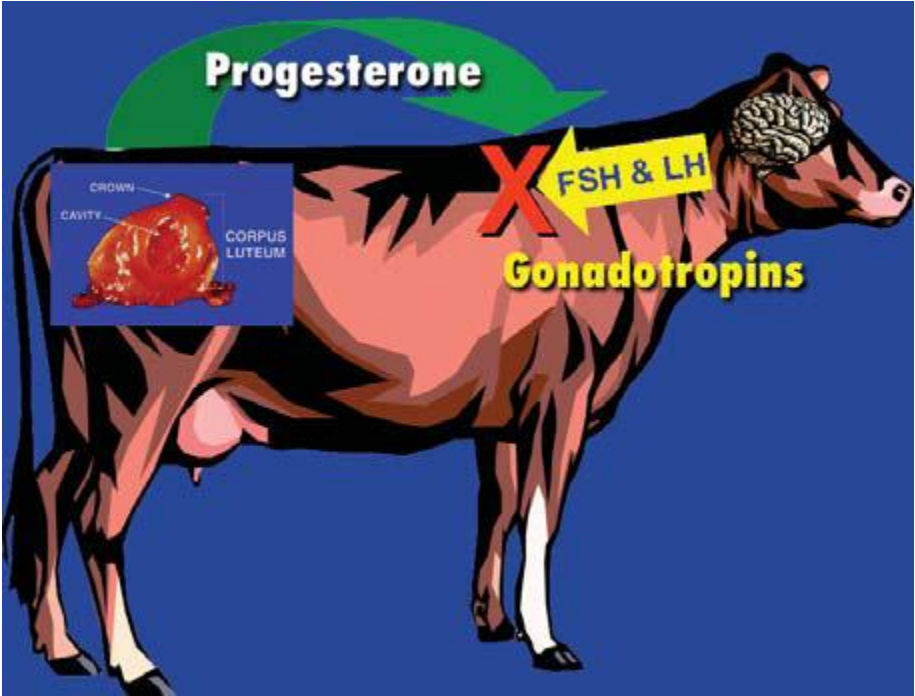
Decompose by bacteria

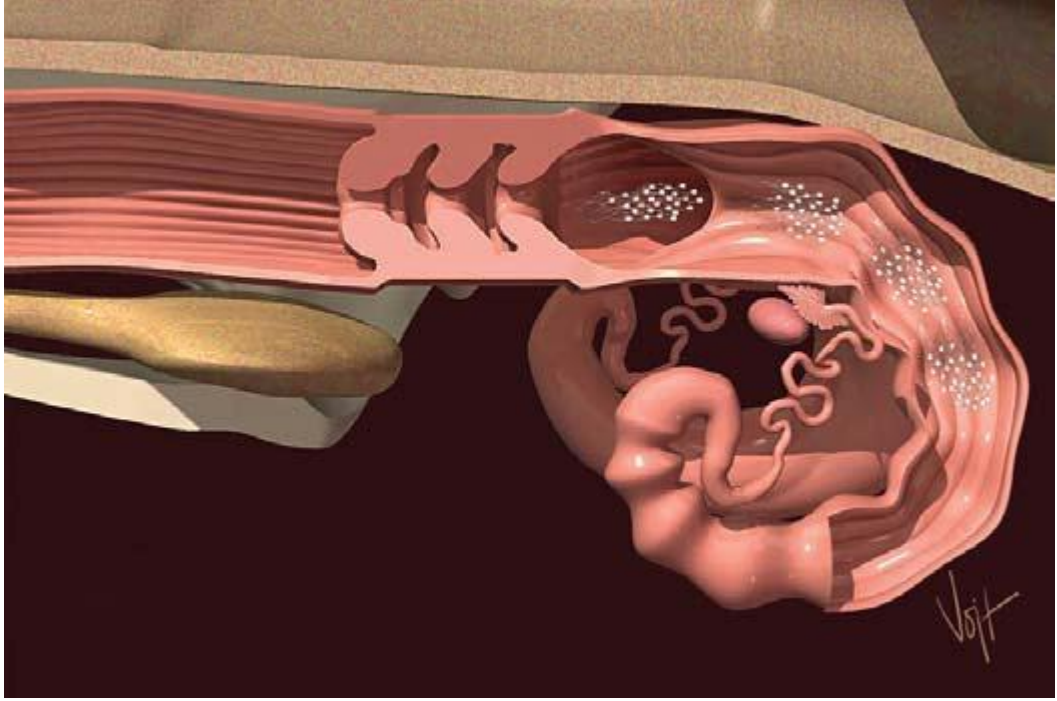
Volatile fatty acid

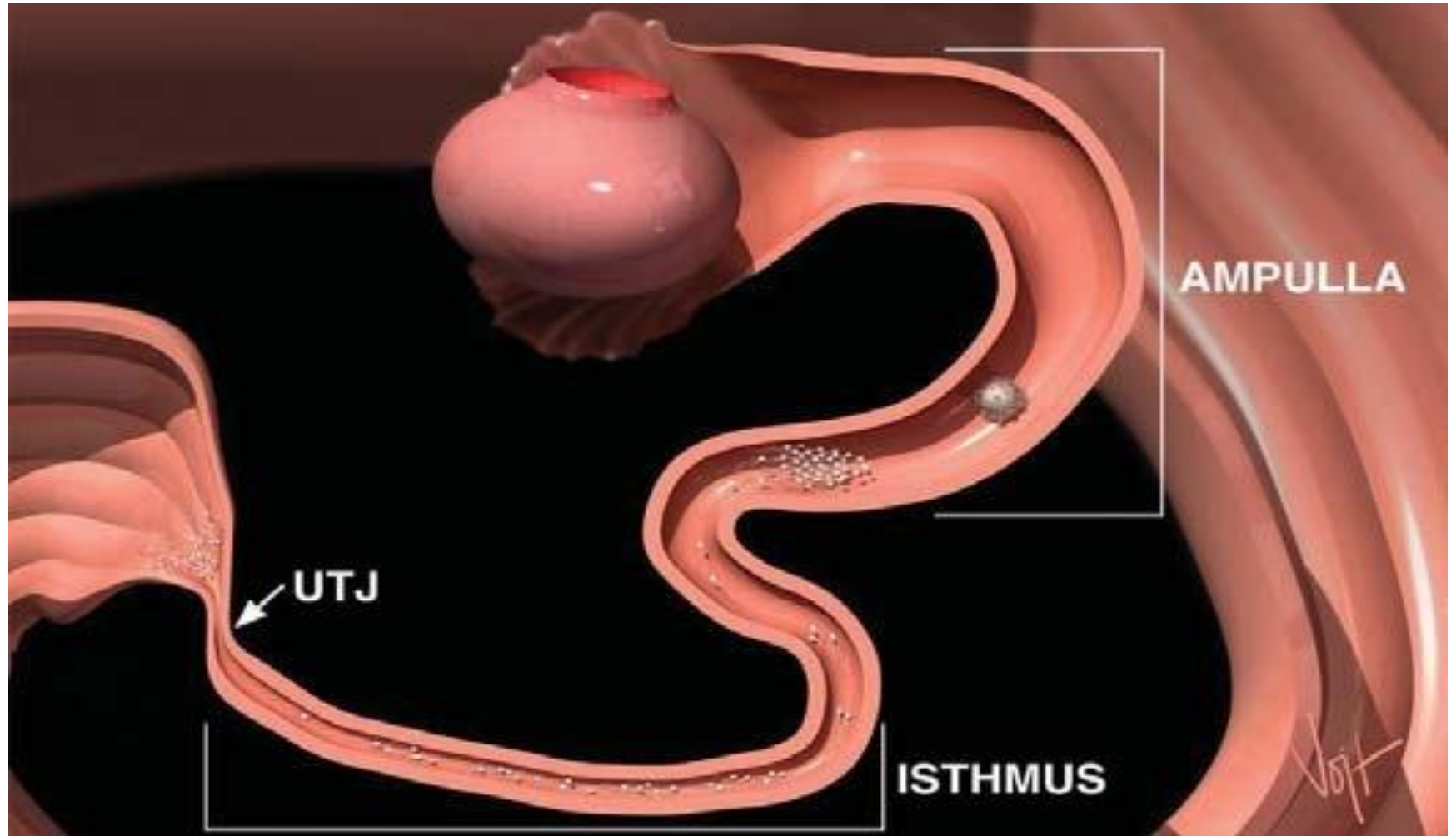
Pole glands

Near the horns

Attract other sex







Pregnancy (gestation period)

It is a condition of a female while youngs are developing within her uterus. The gestation period extends from fertilization of the ovum to the birth.

It includes:

1- fertilization.

2- cleavage..

3- implantation.

4- placentation.

5- continuous growth of the embryo

1- Fertilization

Union of two gametes (sperm and ova) forming zygote.
Only one sperm needed for one ova.

***journey of sperm:** Millions of sperms **deposited during ejaculation** (in vagina) thousands (in isthmus) ,few hundreds arrive in ampulla
Only one sperm make fertilization

Conditions for successful fertilization:

- 1) Healthy ova and sperm.
- 2) Proper time of insemination (mating) with respect to life span to sperm and ova.

3) Capacitation of the sperm by the uterine and fallopian tube fluids(6-7 hrs.)

It is the process by which the sperm undergo certain changes in the female genitalia to acquire the capacity to fertilize the ova. It involve the following:

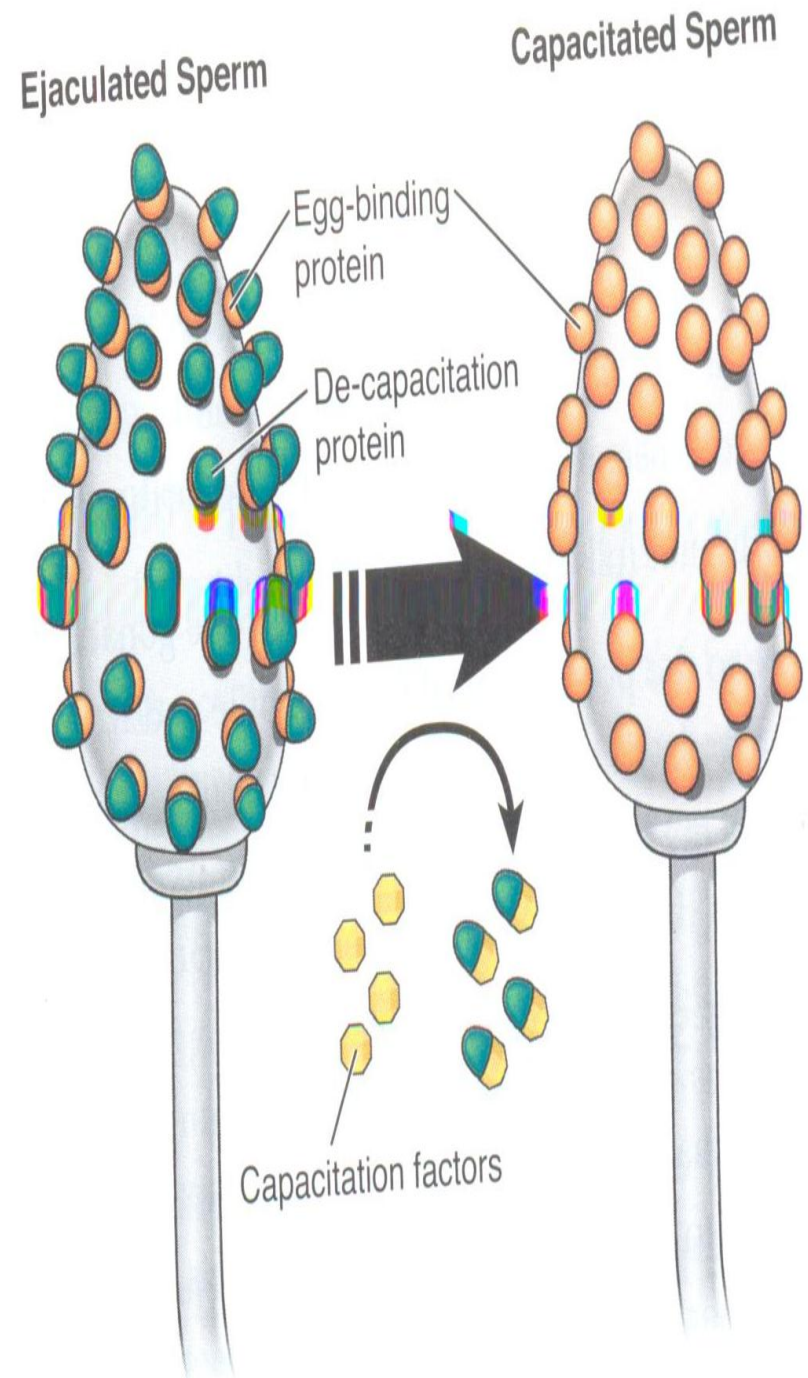
A-removal of macromolecules adsorbed on the sperm from the seminal plasma.

B-removal of the sperm coating antigens by amylase enzyme.

C-inactivation of decapacitation factor.

4-acrosomal reaction: it is the breakdown of the plasma membrane and outer acrosomal membrane and liberation of its contents of enzymes. it starts by the formation of vesicles between them, escape of the acrosome contents and finally loss of the membrane.

The capacitated sperm is prone to the decapacitation factor in the seminal gland or the epididymal fluid. this factor reversibly blocks the union of the sperm and the ovum. It prevents or inhibits the enzymes of the sperms which enable them to digest their passage through the corona radiata cell.

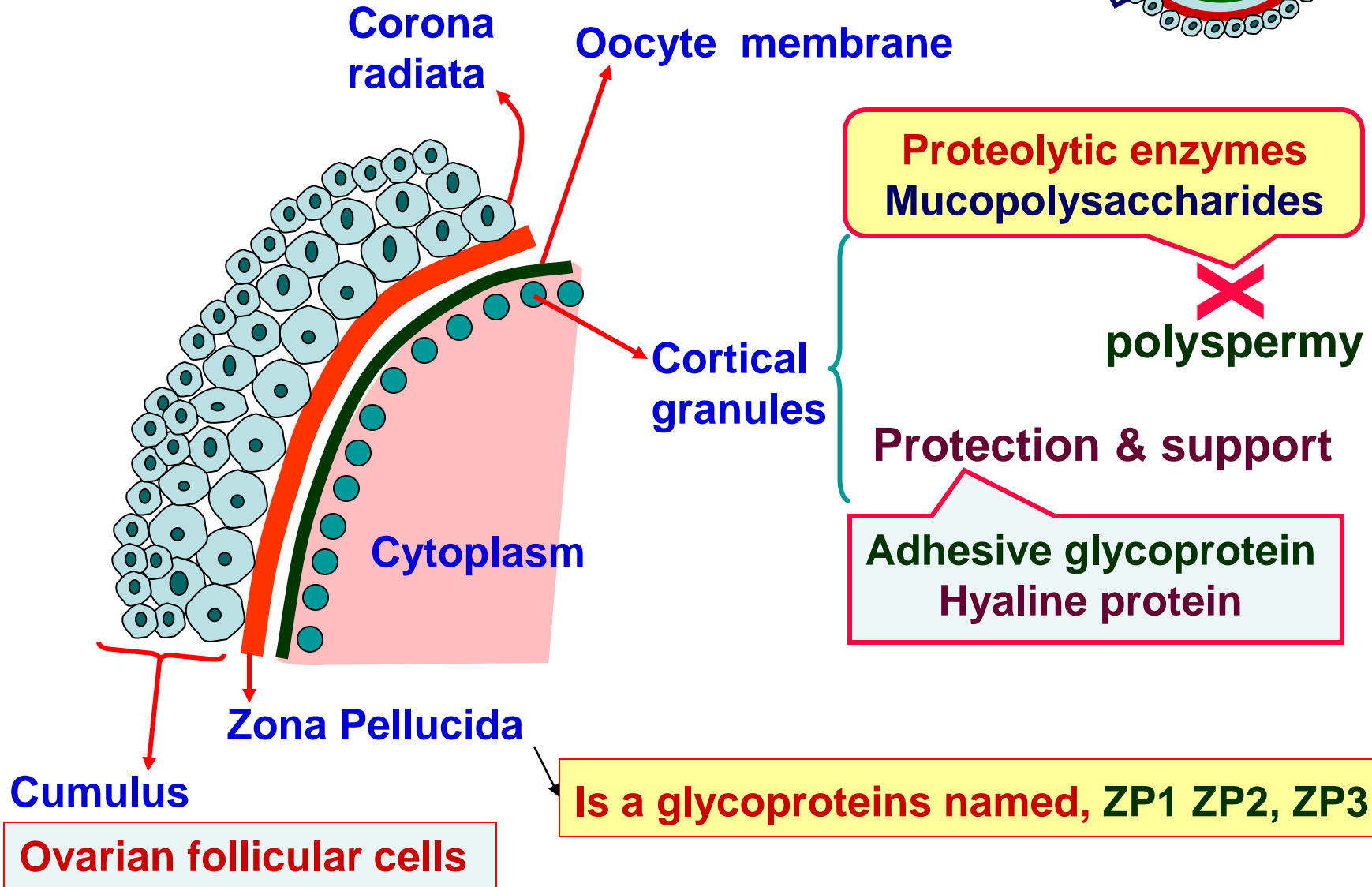
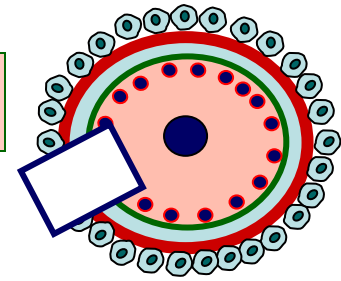


Many sperms are needed to release enough acrosomal enzymes (**acrosin**) to enable one of them to penetrate zona radiata and zona pellucida to fuse with oocyte membrane. Lytic enzymes (**hyaluronidase** to penetrate corona radiata and **proteolytic** for zona pellucida digesting it and permitting flagellar movement of sperm to propel it towards oocyte . Finally the sperm penetrates through the vitelline membrane and the union of gametes is accomplished.

. Fusion between sperm and egg is mediated by protein molecules whose hydrophobic groups merge the sperm and egg plasma membranes. In mammals fertilin proteins in the sperm binds to integrin in the egg and allow membranes to fuse.

Pregnancy

Ovulated oocyte



Fertilization

Receptor recognizing sperm head membrane

ZP3

Receptor activating acrosome reaction

Proteolytic enzymes ← Acrosome

Zona Pellucida

Coritcal granules

Perivitelline space

Oocyte membrane

1 Contact

2

3

Digest ZP

Acrosin

Flagella movement

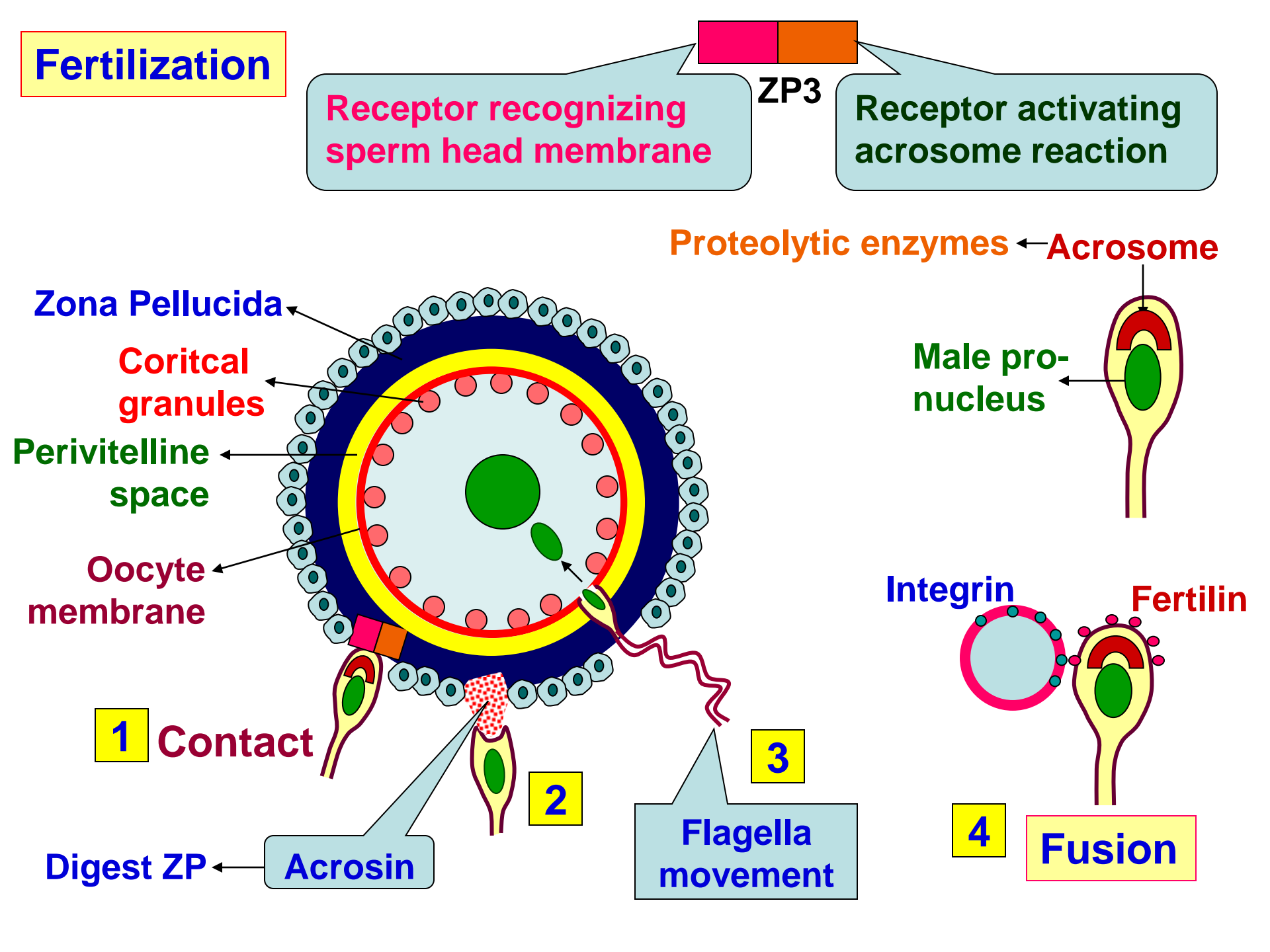
Male pro-nucleus

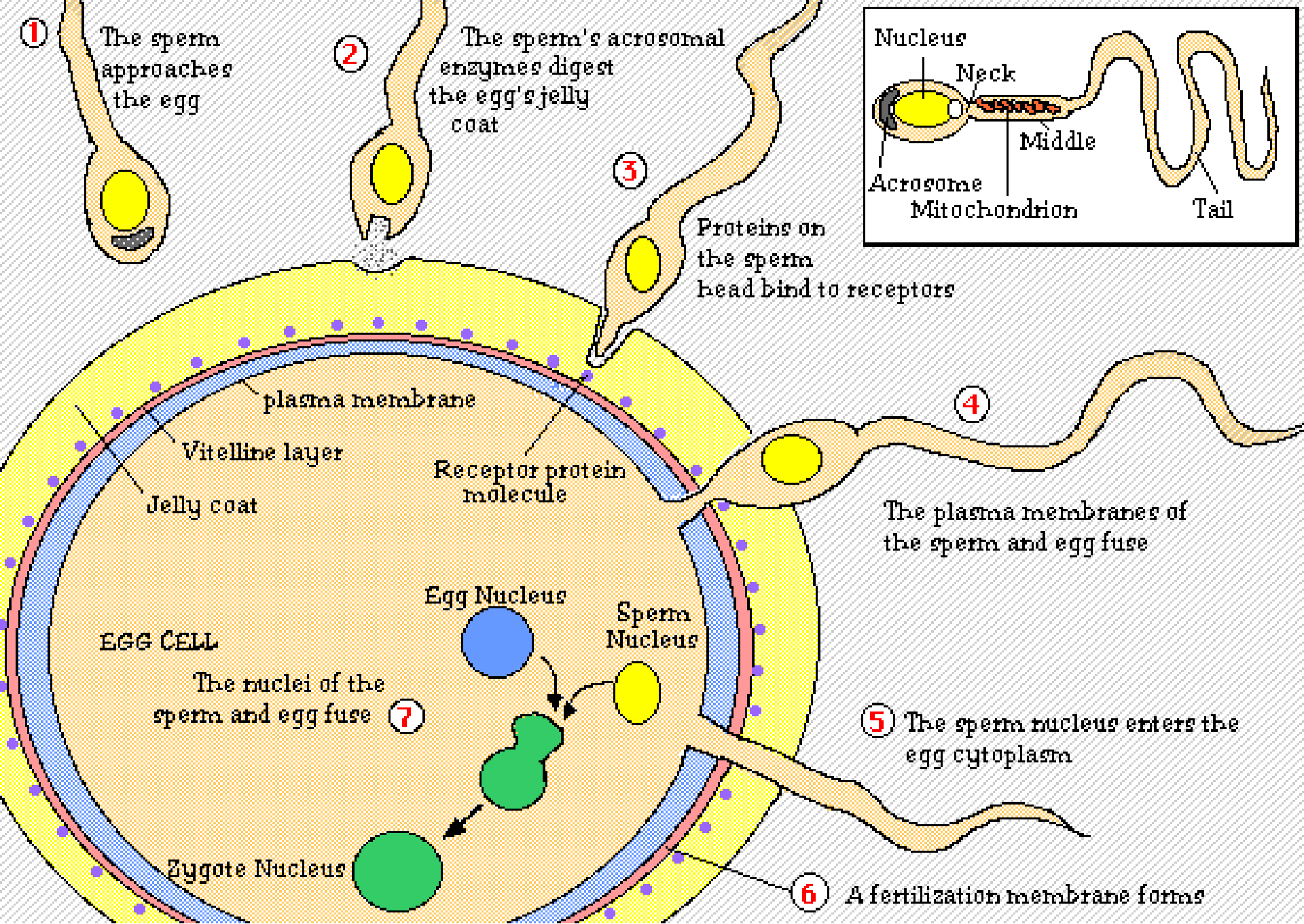
Integrin

Fertilin

4

Fusion





Events occurring after entrance of the sperm:

1-zona pellucida reaction:

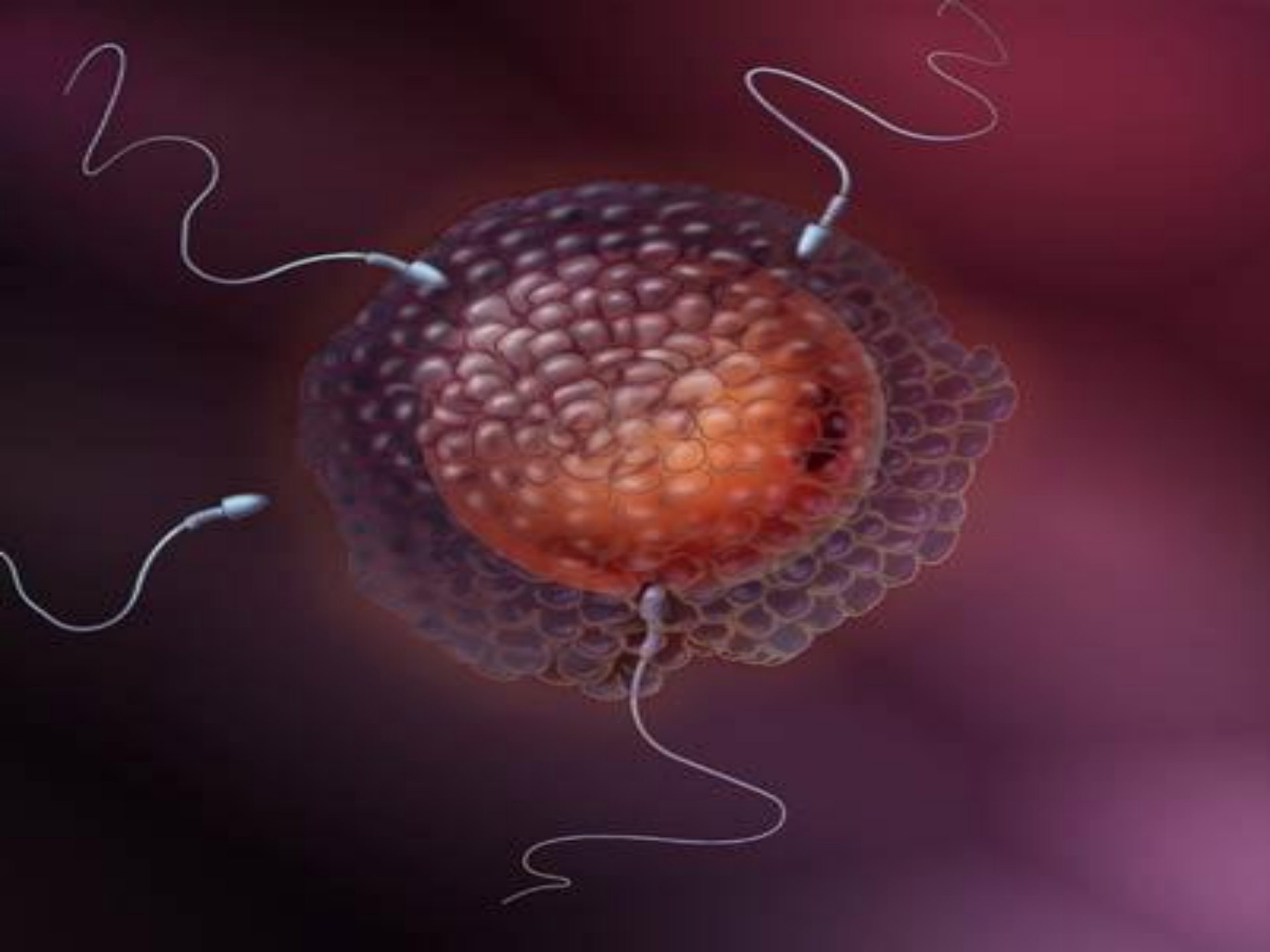
The contact between sperm and oocyte responsible for releasing of cortical granules which is liberated by exocytosis aided by Ca^{++} resulting in slow block to polyspermy.

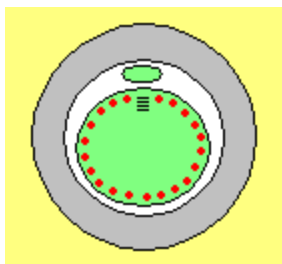
2-vitelline membrane reaction (fast block):

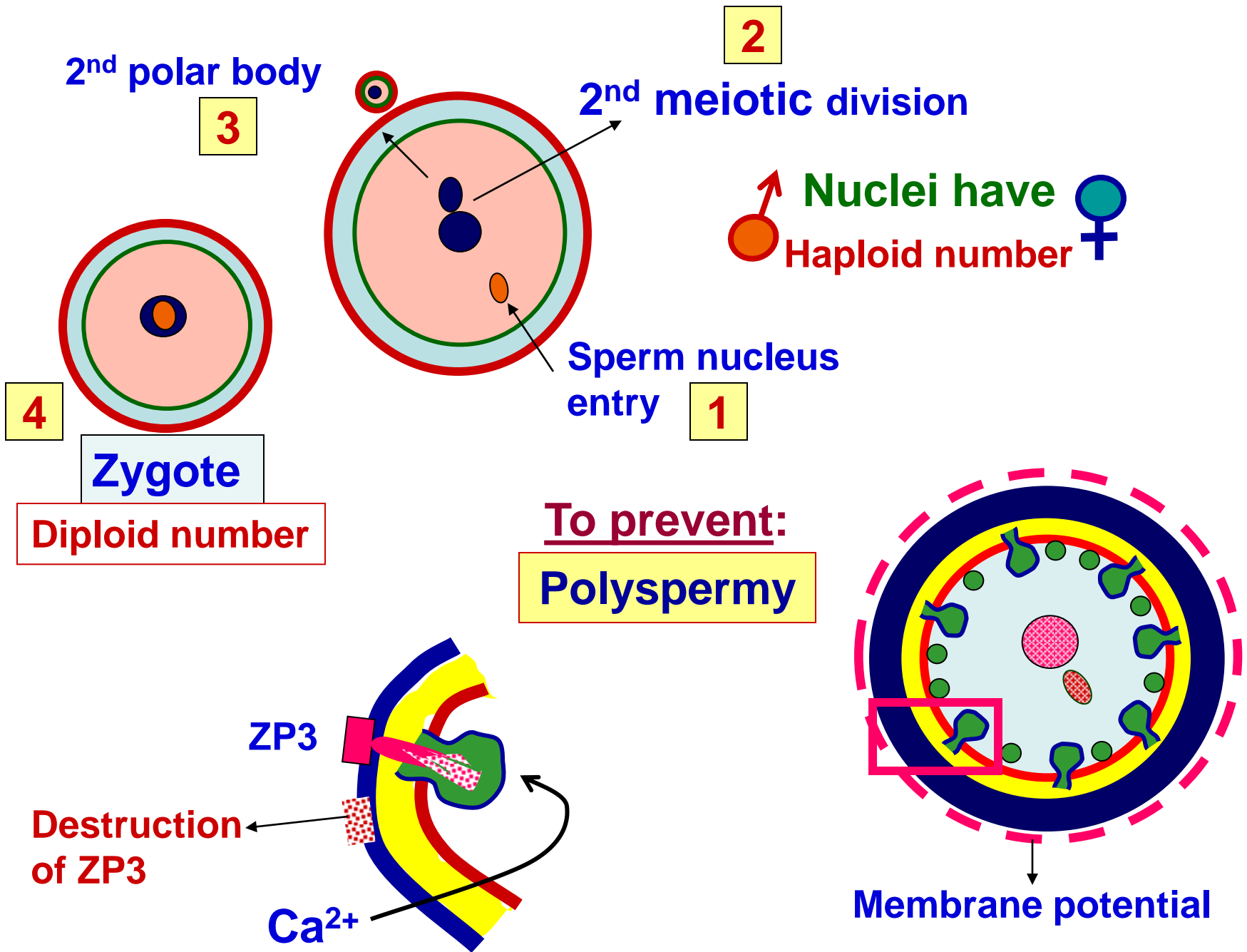
Is resulting from thickening and electrical depolarization of the membrane . The electrical charges on the surface of the ovum block the entry of the other sperms.

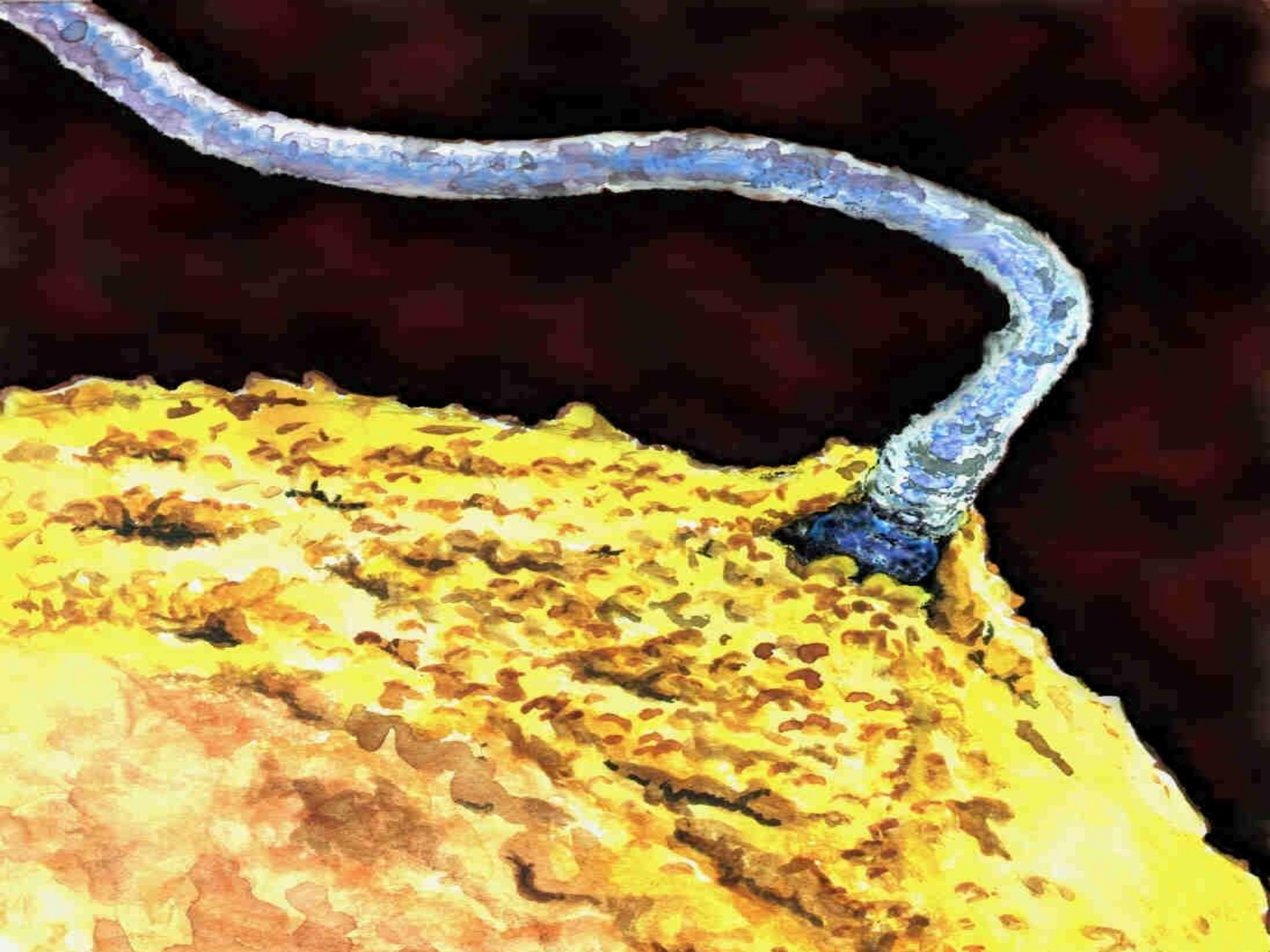
3-formation of pronuclei, meiosis II and the zygote:

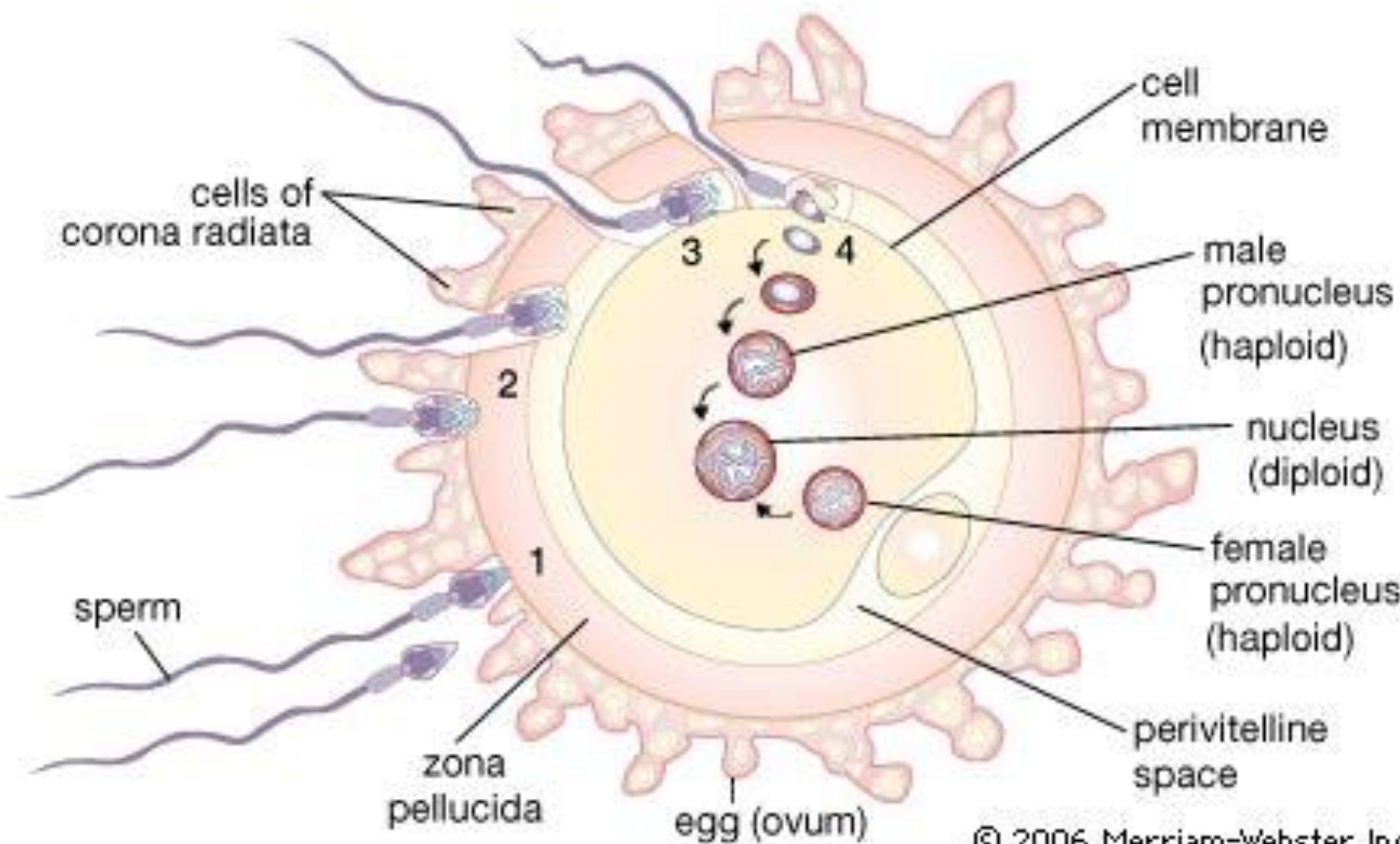
After entrance of the sperm into the ovum, the tail is shed and the nucleus in the develops into a structure called male pronucleus The entry of sperm nucleus triggers secondary oocyte to complete meiosis forming second polar body. The nucleus of the ovum develops into a female pronucleus, and then migrates to the periphery to fuse together with the male pronucleus to form a segmentation nucleus (zygote)











cells of corona radiata

cell membrane

male pronucleus (haploid)

nucleus (diploid)

female pronucleus (haploid)

perivitelline space

sperm

zona pellucida

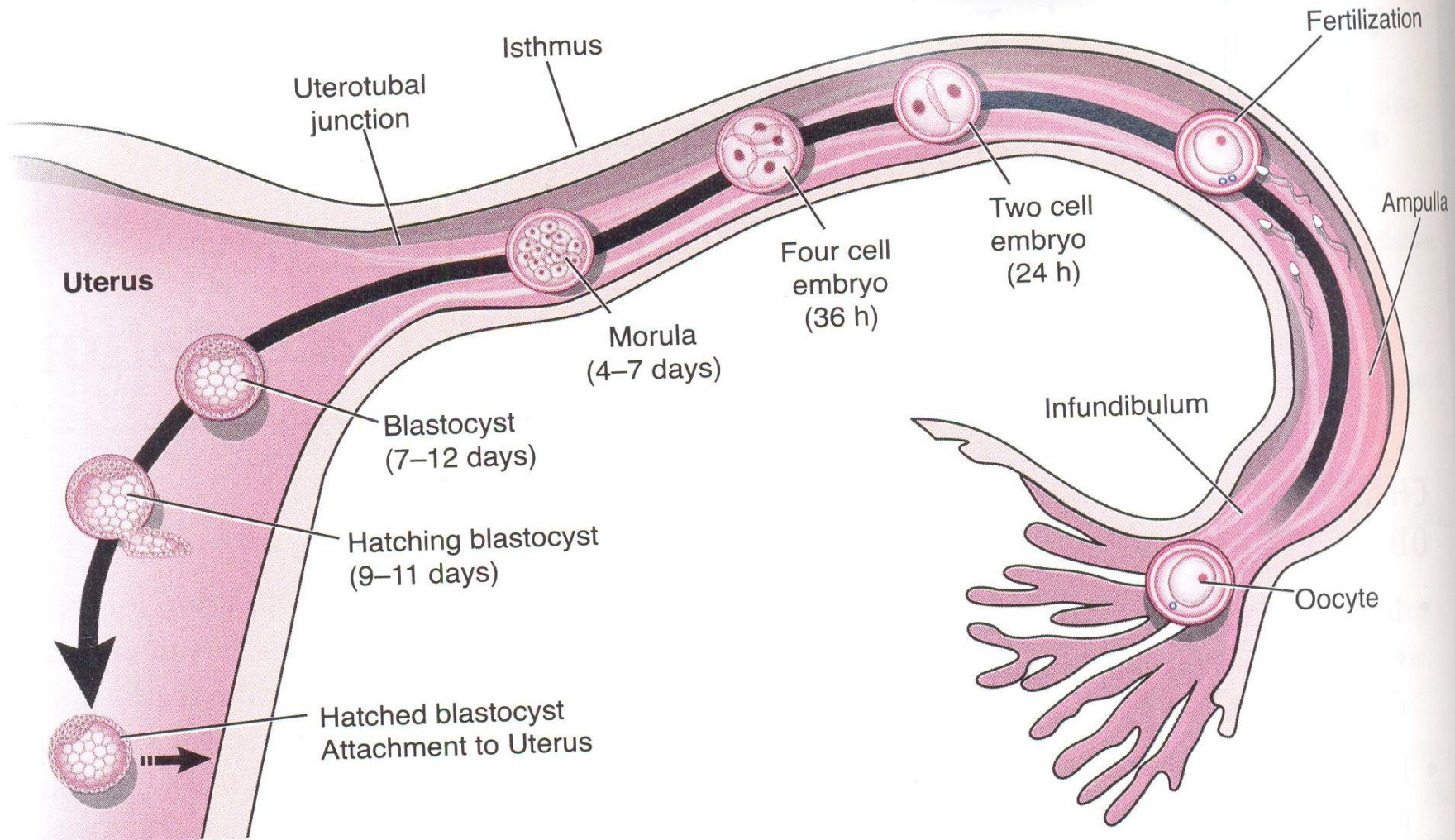
egg (ovum)

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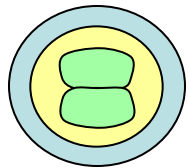
Cleavage:

1-formation of the morula

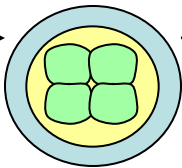
2-development of blastula



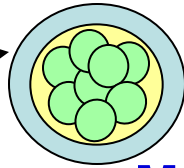
Embryonic Development



2 cell stage

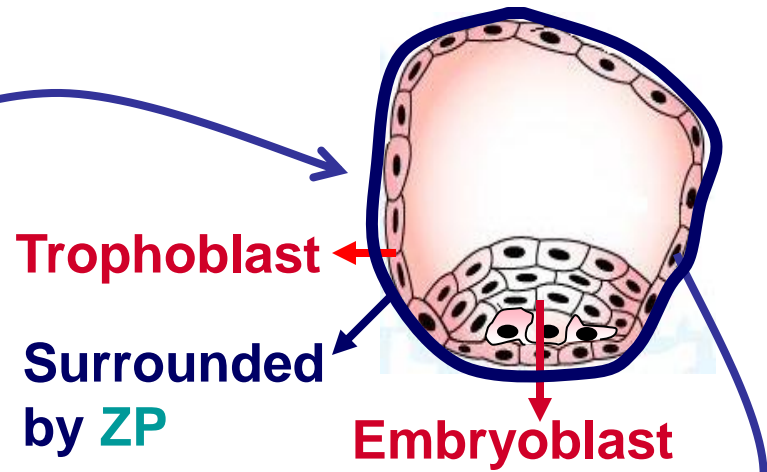


4 cell stage



Morula

Ball of cells



Trophoblast

Surrounded by ZP

Embryoblast

Implantation

Primates, dog, cat, rabbit, rat

Invasive implantation

Cow, mare, sheep, sow

NON-invasive implantation

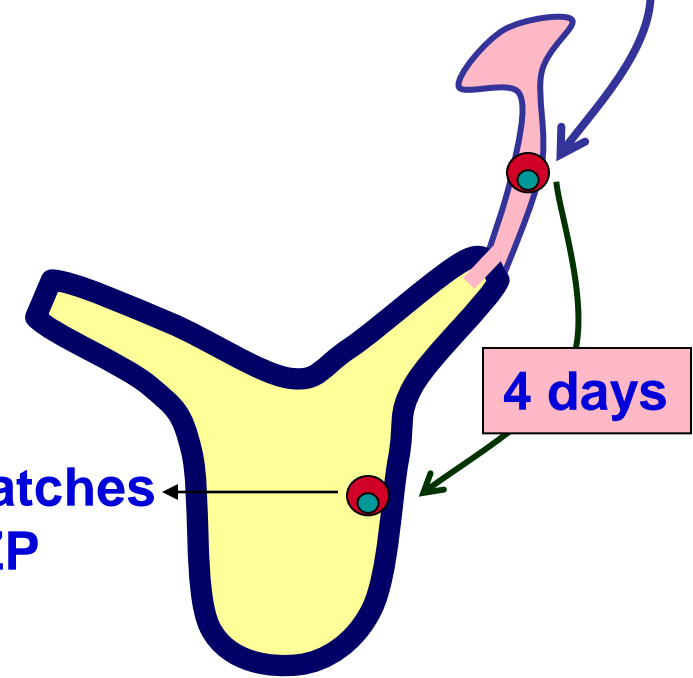
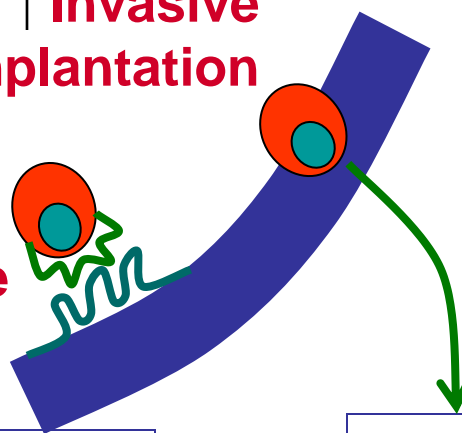
Fetus & maternal layers attaches together

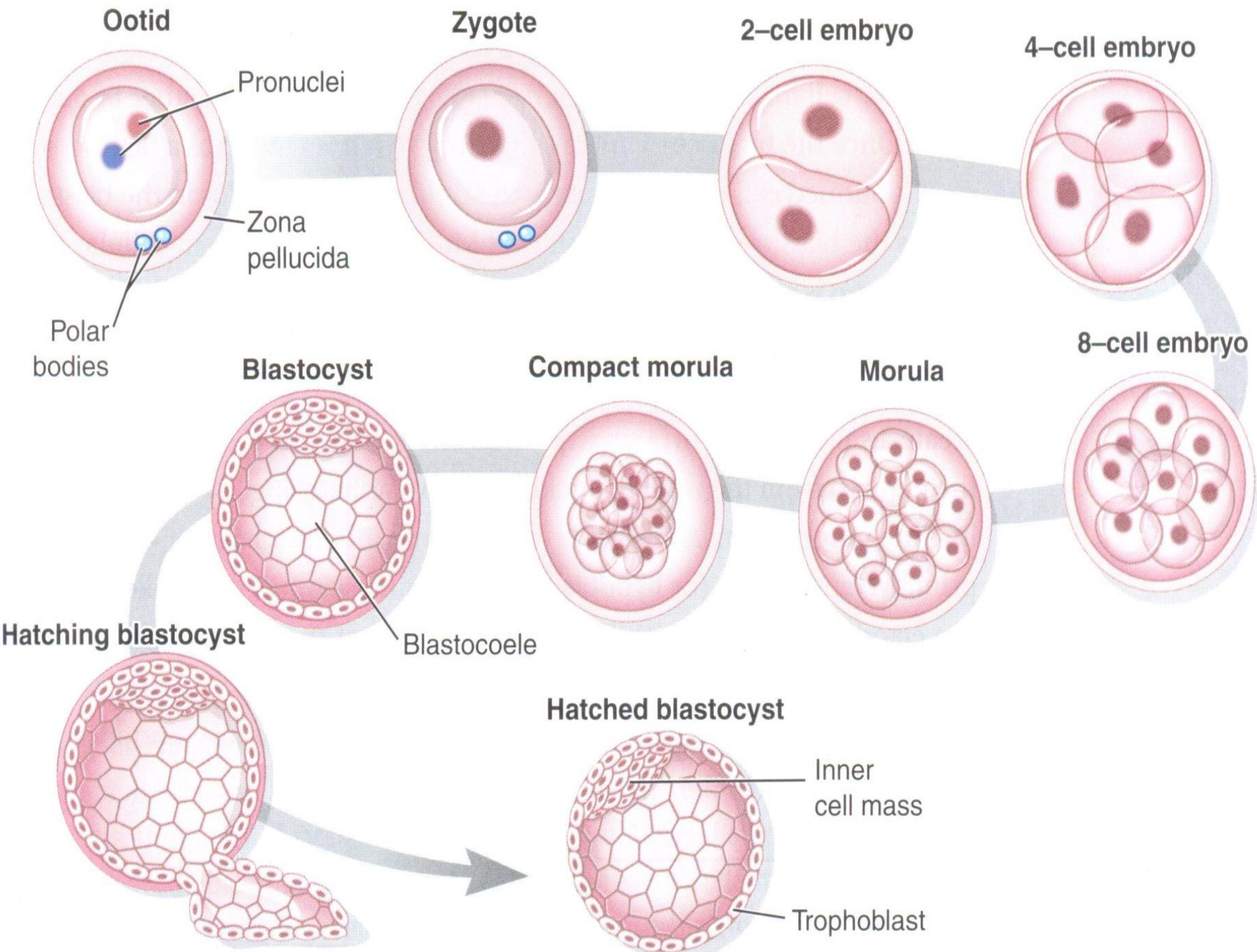
Fetus erode uterine wall

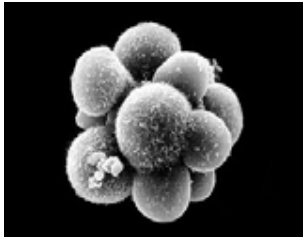
Ova hatches from ZP

4 days

Fetus implants in uterine wall







The morula

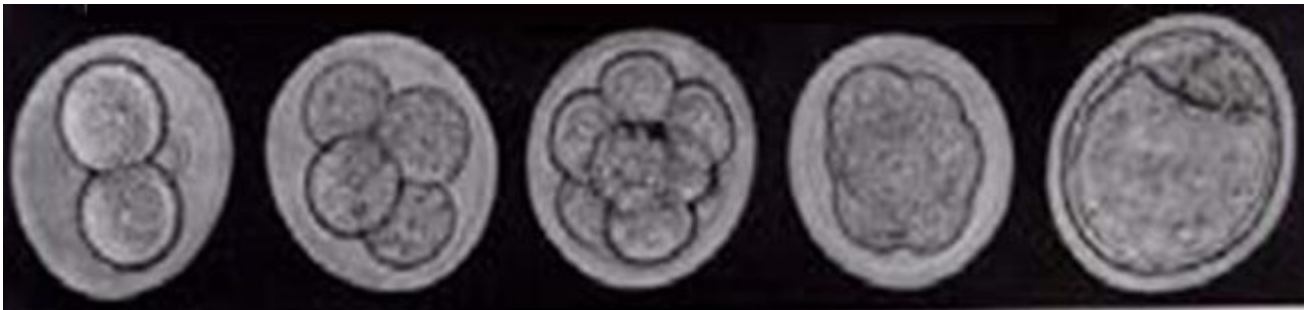
The blastocyst

Trophoblast - will form the placenta



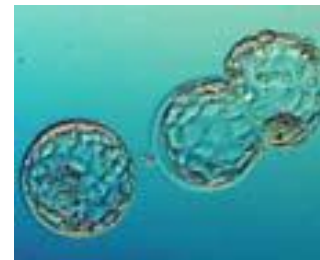
Inner cell mass - will form the embryo

Pre-implantation embryo developmental stages



Cleavage

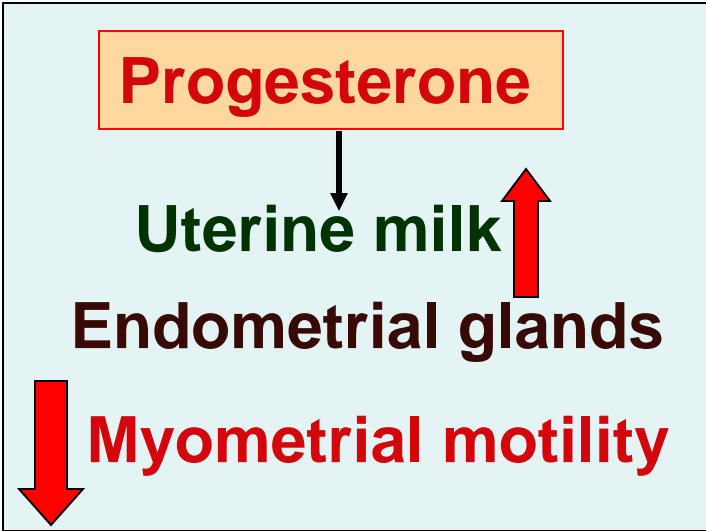
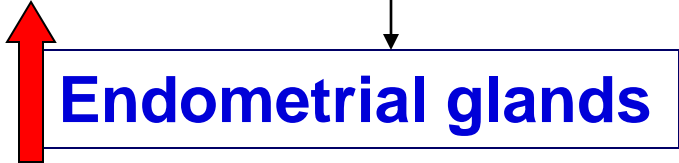
Hatching of blastocyst



Monozygotic (identical) twinning may occur at this stage

Hormones & implantation

Estrogen



Embryonic nutrition



Placentation

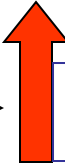
Fetal part
Chorion

Maternal part
Decidua basalis Uterus

Functions of the Placenta

Gas transport

Fetal Hb



O₂ affinity

Nutritive

By diffusion

All nutrients

Excretion

Of all waste products of Mb

Barrier

Incomplete barrier

Substances pass across:
Hormones, IgG,
sedatives, some viruses

Substances don't pass across:
Large molecules like: Insulin,
heparin, and antibodies in herbivore

Herbivore feti born **without ANY maternal** antibodies in their blood

Table 10-11. The main differences between hCG and eCG

hCG (human and primates)	eCG, PMSG, (equines only)
Produced from the trophoblast layer of the embedded fertilized ova.	Produced from the cuplic structures in the endometrium.
Produced 10 days after fertilization; reaches maximum levels after 10 weeks; then decline and remain low	Produced 30 days after implantation; reaches maximum at mid-gestation
Can be detected in both urine and serum samples	Can be detected only in serum samples
It is LH in nature and weak FSH effect	It is FSH in nature
<p data-bbox="125 649 280 692">Actions:</p> <ol data-bbox="125 706 1052 1392" style="list-style-type: none"> <li data-bbox="125 706 589 763">1. It prevents luteolysis <li data-bbox="125 763 840 821">2. Stimulates corpus luteum growth <li data-bbox="125 821 1052 1035">3. Stimulates corpus luteum to secrete estrogen and progesterone till the 10th week of gestation for continual endometrial growth. <li data-bbox="125 1035 1052 1192">4. It acts on placenta itself from the 4th month to secrete estrogen and progesterone. <li data-bbox="125 1192 1052 1392">5. Suppresses maternal immune function i.e. reduces the possibility of fetus immunorejection 	<p data-bbox="1052 692 1226 735">Actions:</p> <ol data-bbox="1052 749 1864 1392" style="list-style-type: none"> <li data-bbox="1052 749 1497 806">1. It prevent luteolysis <li data-bbox="1052 806 1864 1392">2. Since it is FSH in nature, so it may stimulate follicular growth during pregnancy, which leads to increase in estrogen secretion and appearance of estrus during pregnancy. Secondary corpus luteum will be formed when these follicles ovulate and more progesterone is produced for further pregnancy maintenance.

Placental hormones

Chorionic gonadotropines

hCG in primates

Like **LH**

10 days – 10 weeks

Detected in **urine** and serum

~~Luteolysis~~

Luteotropic

Progesterone

Affect placenta

Estrogen

Progesterone

Maternal immune activity

Fetal rejection

Chorionic gonadotropines

PMSG

eCG in equines

Like **FSH**

30 days – mid-gestation

Detected in serum **only**

Follicular growth

Estrogen

Signs of estrus

Secondary CL

Progesterone

Placental lactogen

Chorionic somatomammotropin

GH-like in primates

Prolactin-like in ruminants

Functions

Maturation of mammary gland

Energy production

Fetal & placental growth

Lipolysis

Nitrogen, K and Ca retention

Relaxin

CL, uterus, placenta

Relax pubic symphysis

Dilates the cervix

Progesterone

Estrogen

CRH, TRH, GHRH, ACTH, TSH, Activates Vit.D

Maternal Recognition of Pregnancy

A critical need arises early in the gestation for the mother to recognize that she is pregnant, why? t

Progesterone levels in maternal blood must remain at high level to keep endometrial maintenance in a state conducive to embryonic survival.

Maternal recognition of pregnancy does not involve any type of conscious recognition by the mother, Instead. The concepts must signal its presence to the mother in order to prevent luteolysis of the corpus luteum.

The need to prolong luteal life is accomplished by:

1-production of positive luteotropic factors

2-prevention of normal luteolytic factors

Maternal Recognition of Pregnancy

6-7 days of fertilization

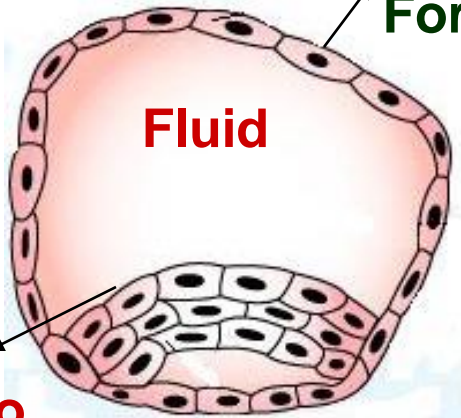
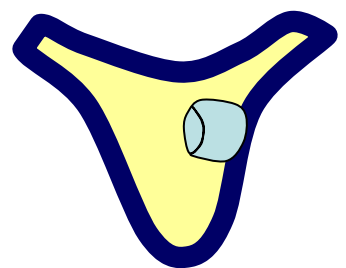
In primates

Blastocyst

Trophoblast

Outer cells
Form placenta

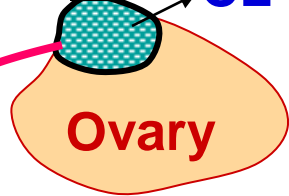
hCG



Inner cell mass
Form the embryo

LH receptor

CL



Progesterone

Ovary

Prolong CL life

In animals

Extra CL(s)

Endometrial cups

Equines

Cattle & sheep

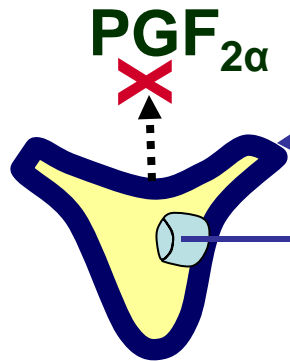
Prolong CL life

eCG

Estrogen

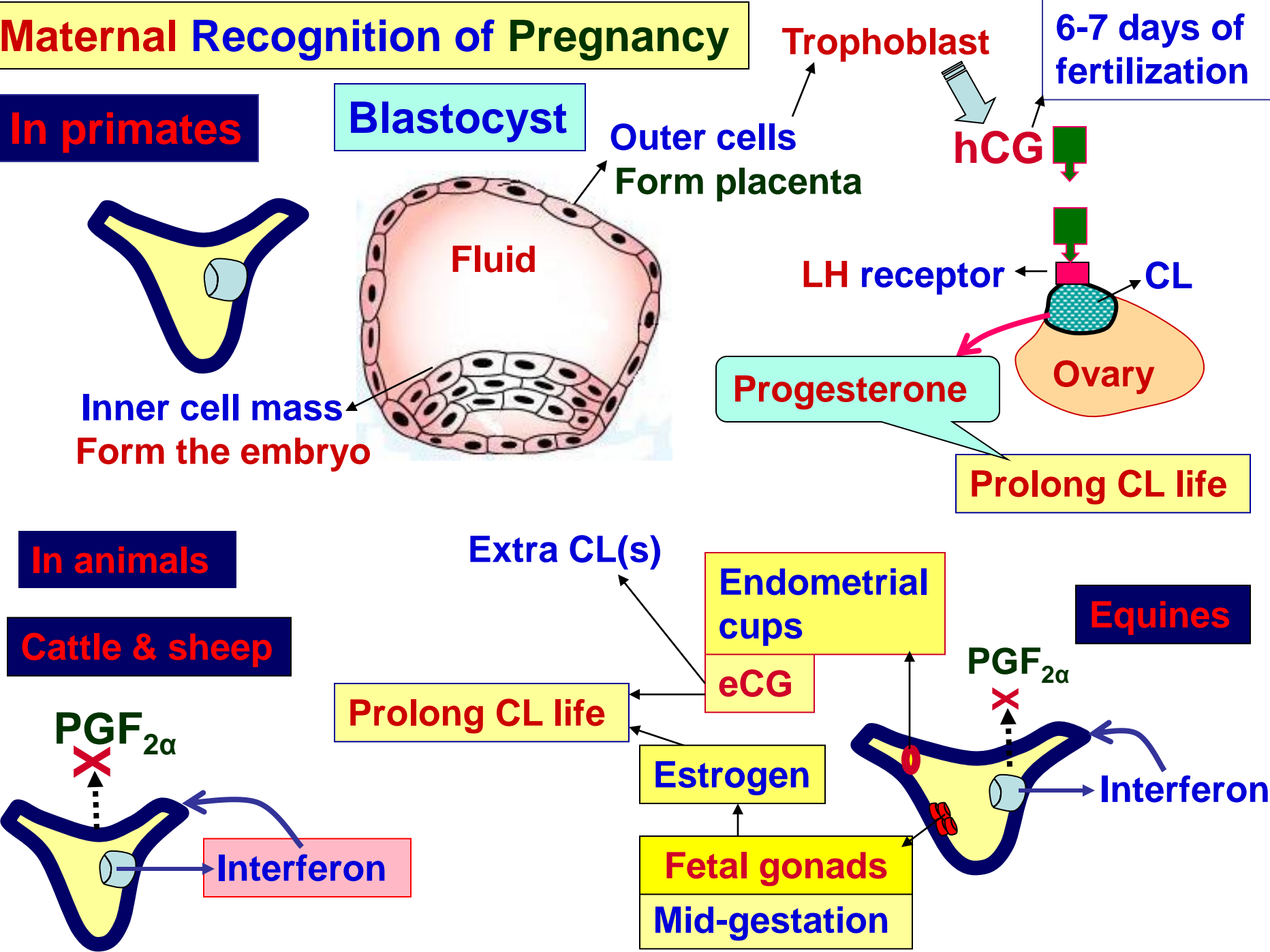
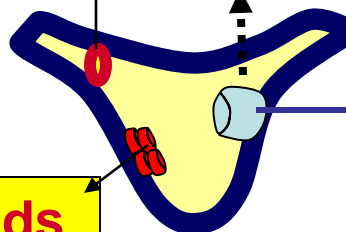
PGF_{2α}

Interferon



Interferon

Fetal gonads
Mid-gestation



In cats and bitch:

In cats,

the corpus luteum lasts for 35-45 days after ovulation, whether pregnant or not. Placenta extends luteal function for the rest of pregnancy (63 days).

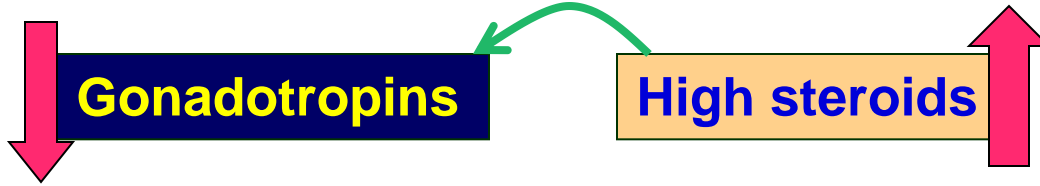
In bitch:

The presence of conceptus prolongs the luteal life.

Time the placenta take over (totally) the progesterone production from CL

	Time of placental take-over	Gestation Length (days)
Primates	5-8 <u>weeks</u>	Differs
Cow	150 days	270 days
Ewe	50 days	150 days
Mare	70 days	340 days
Cat	45 days	63 days
Goat	Totally on CL	150 days
Sow	Totally on CL	115 days
Rabbit	Totally on CL	30 days

Hormonal control of pregnancy



Progesterone blocks effect of estrogen on myometrial activity

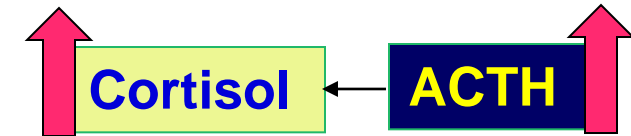
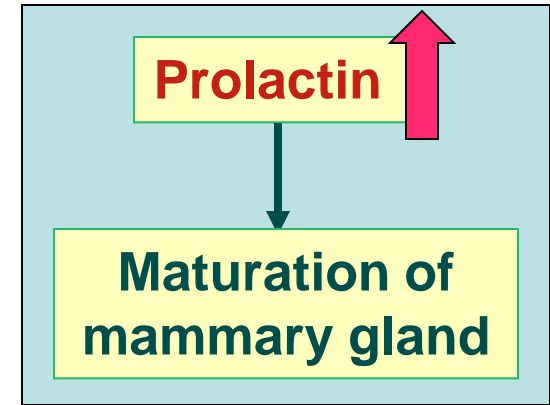
High estrogen

Thyroxin & cortisol binding proteins

Activates Renin-angiotensin system

Aldosterone

BMR

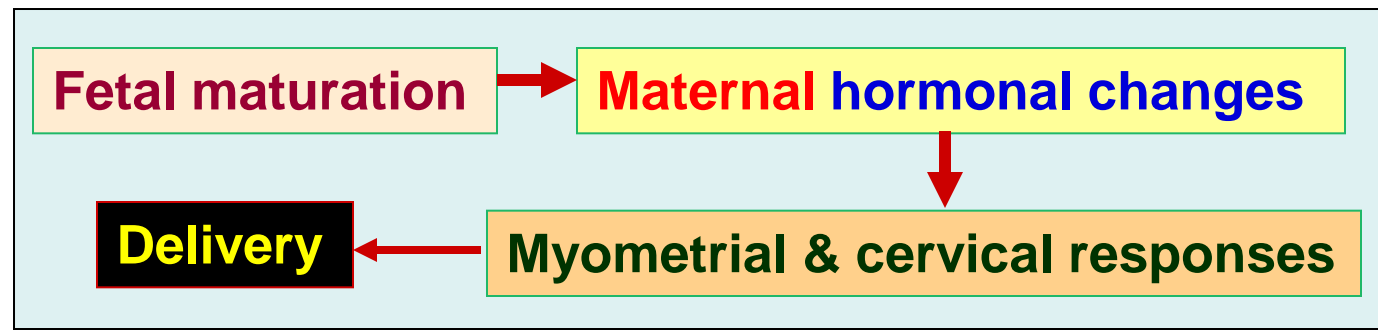


Parathormone & Vitamin D

Calcium deposition in bone

Fetal needs

Parturition



Goes into 3 stages

1

Preparatory stage

Maternal and fetal hormonal changes

2

Expulsive stage

Open the cervix & strong myometrial contractions

Expulsion of the fetus

3

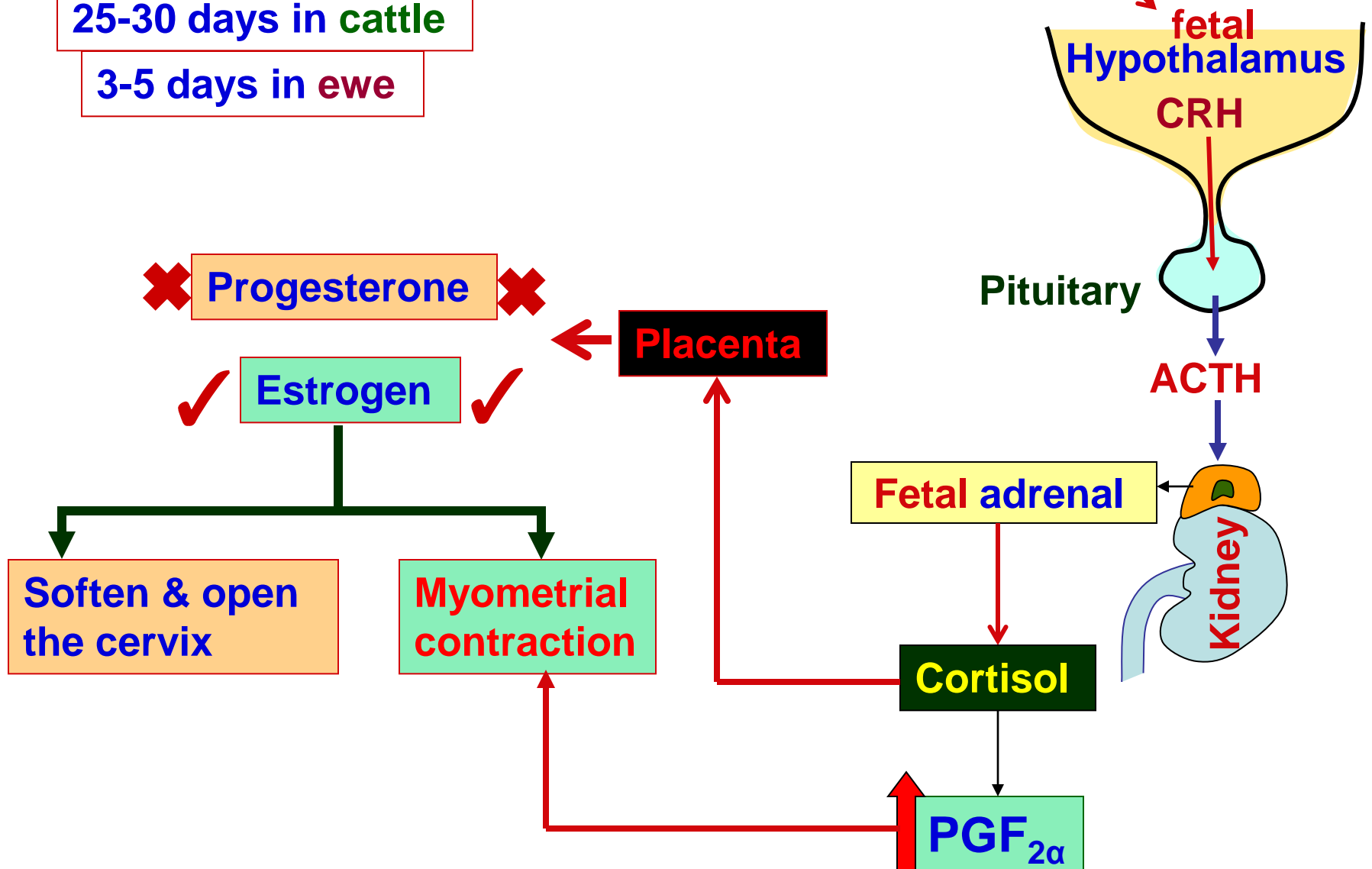
Expulsion of the fetal membranes

Preparatory stage

25-30 days in **cattle**

3-5 days in **ewe**

Fetal maturation

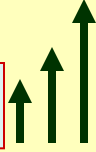


25-30 days in **cattle**

3-5 days in **ewe**

During last **trimester**
of pregnancy

Estrogen



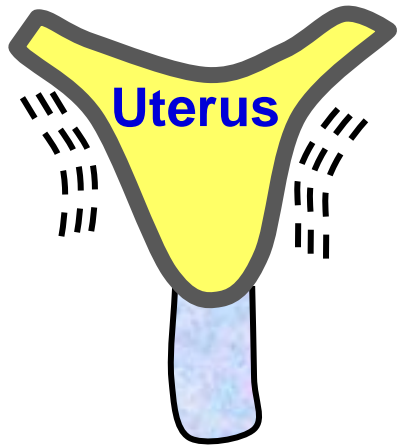
Fetal **Hypothalamus-pituitary-adrenal** axis

Matures:

Estrogen : progesterone **ratio**



Placenta form estrogen
instead of progesterone



Cervix

Fetal **cortisol**



Placenta

17- hydroxylase
& 17-20 lyase ✓

Progesterone



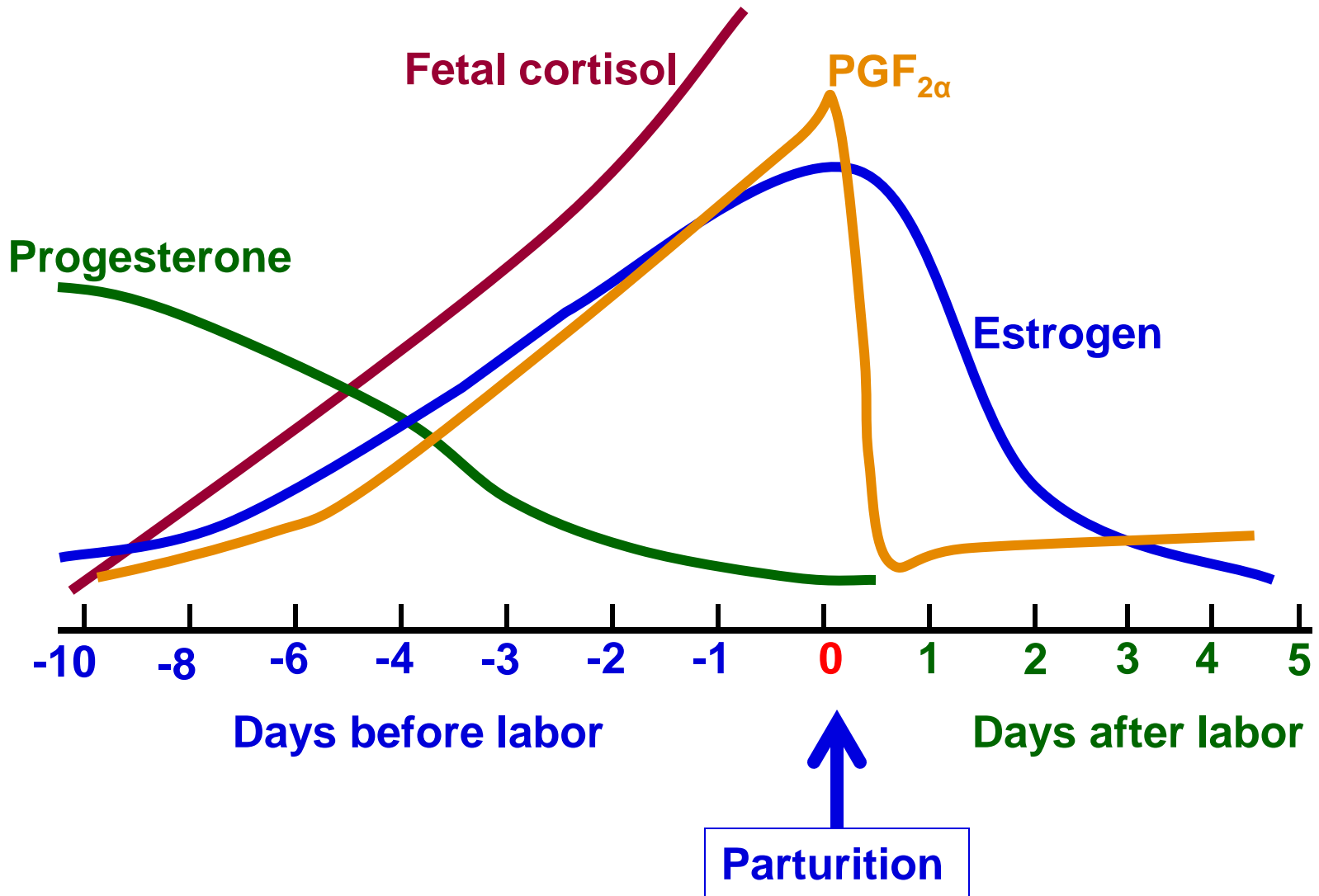
Estrogen

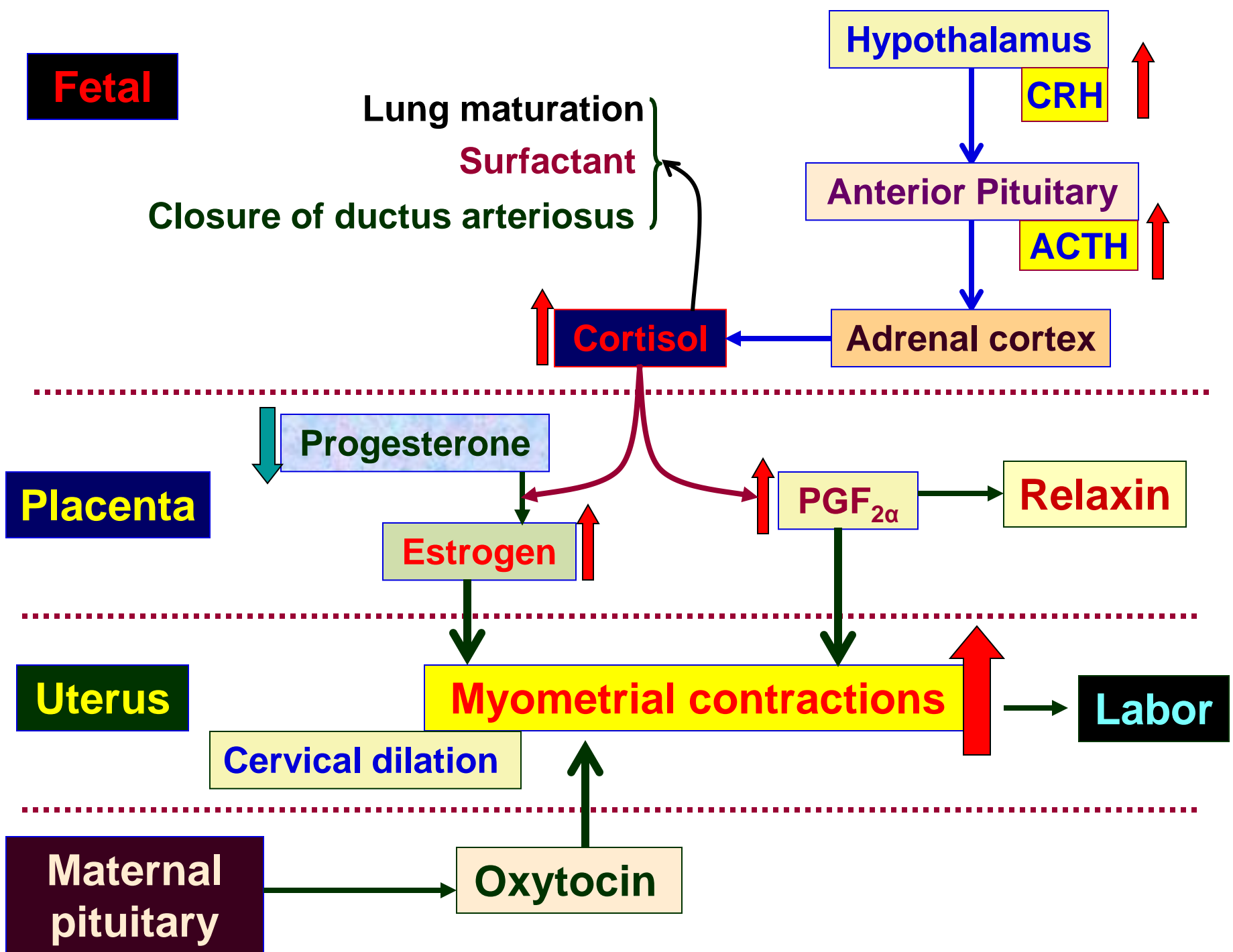


PGF_{2α}



Hormonal changes leading to parturition





In primates

Fetal

Fetal Adrenal cortex

Dehydroepiandrostenone

DHEA

Estrogen

Pregnanolone

Placenta

Deficient in some enzymes necessary for :

synthesizing estrogen from progesterone

Relaxin

Sensitizing the uterus for the action of:

Oxytocin

PGF_{2α}

Synthesis of sex steroids

Placenta

Cholesterol

Pregnanolone

Progesterone



Dehydroepiandrosterone

Androstenedione

Testosterone

Estrogen

Fetal adrenal

Pregnanolone

Dehydroepiandrosterone

Placenta

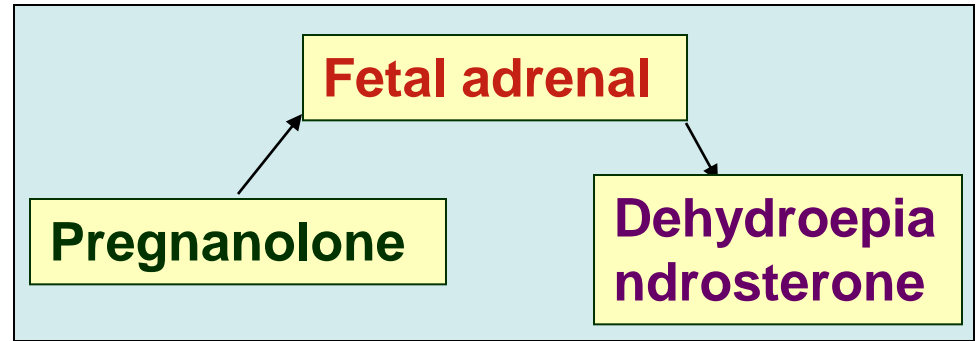
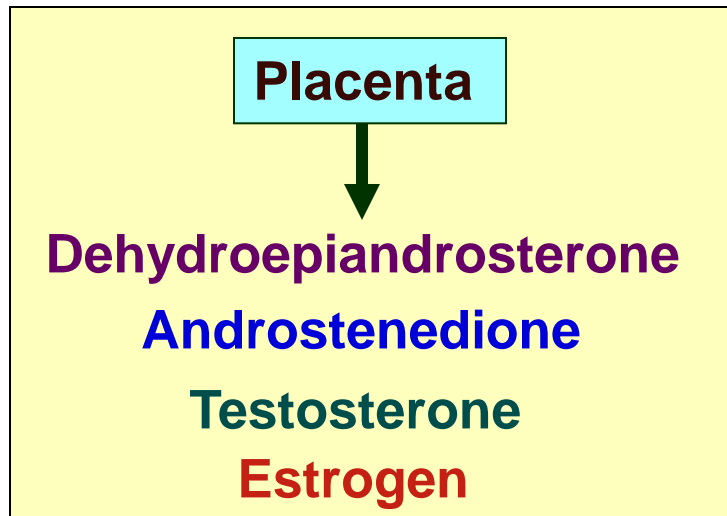
Dehydroepiandrosterone

Androstenedione

Testosterone

Estrogen

primates



In Equines

Fetal

Fetal Gonads

Dehydroepiandrostenone

DHEA

Estrogen

Pregnanolone

Placenta

Deficient in some enzymes necessary for :

synthesizing estrogen from progesterone

Relaxin

Sensitizing the uterus for the action of:

Oxytocin

PGF_{2α}

In Goat

CL support pregnancy during the whole pregnancy period

Fetal

Fetal Adrenal cortex

Cortisol

Estrogen

PGF_{2α}

Placenta

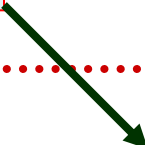
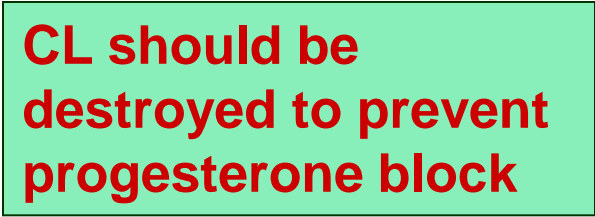
Maternal ovary

CL should be destroyed to prevent progesterone block

Luteolysis

Progesterone

Ovary



Mechanical changes :the uterus is converted from quiescence to a contractile organ. The cervix relaxes and opens to allow the fetus to be delivered.

Thus, the mechanical changes include; increased the velocity and amplitude of myometrial contractions and cervical ripening or softening.

Both $\text{PGF}_2\alpha$ and oxytocin are the target hormones regulate these changes.

Role of $\text{PGF}_2\alpha$:

Liberates Ca from its storehouse to bind with actin –myosin proteins to initiate uterine contraction.

Triggers a powerful uterine and abdominal contraction

Decreasing and loosening the collagen bundle in the cervix resulting in dilatation of cervical canal.

Stimulate relaxin hormone release

Luteolysis.

Role of oxytocin:

Small amount of oxytocin begins to be released during the first stage (dilation of the cervix), and maximum levels occur at the time when fetus head emerges from the vulva during the second stage (fergusson reflex)

Stages of parturition

First stage: it involves presentation of the fetus at the internal os of the cervix. Once the cervix opens and the fetus passes into the pelvic canal, myometrial contractions become less important for delivery; abdominal muscle, becomes the main force involved in the delivery process.

Second stage (expulsion stage)

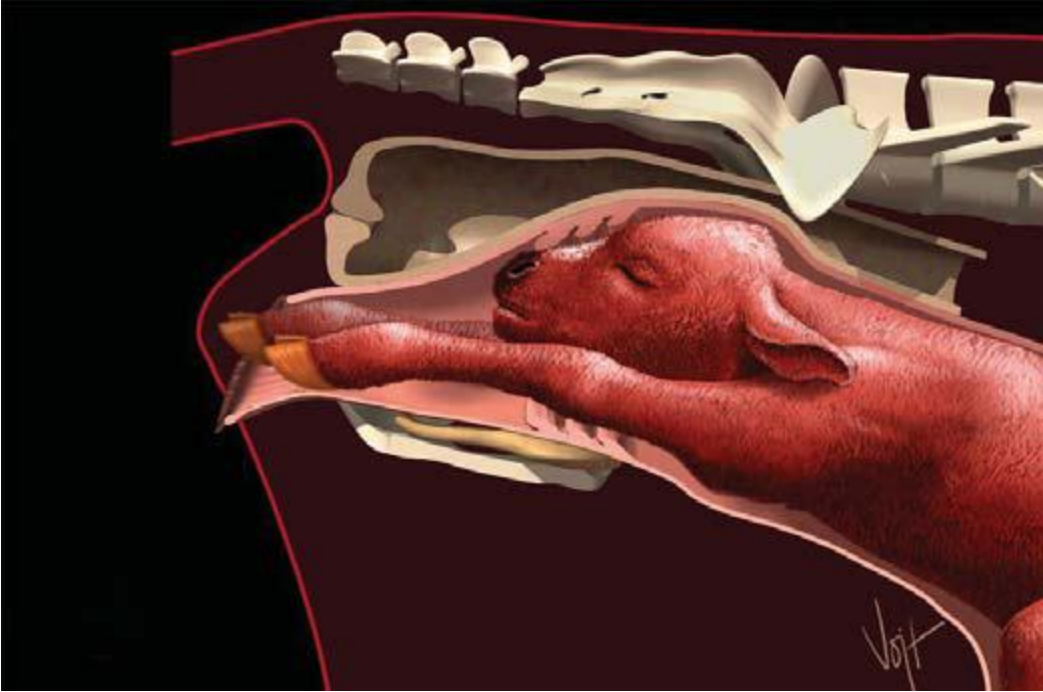
Third stage (placental expulsion stage)



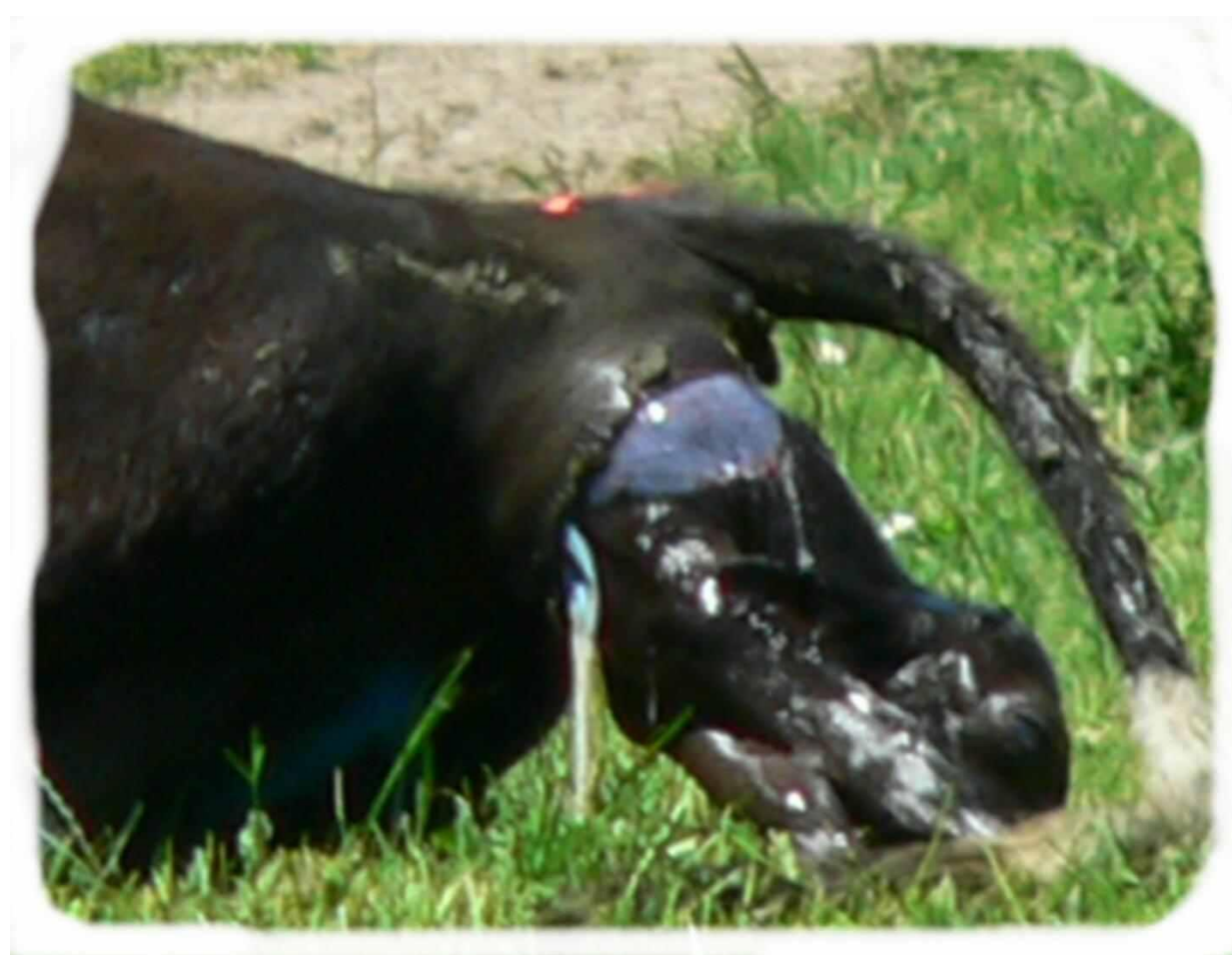


















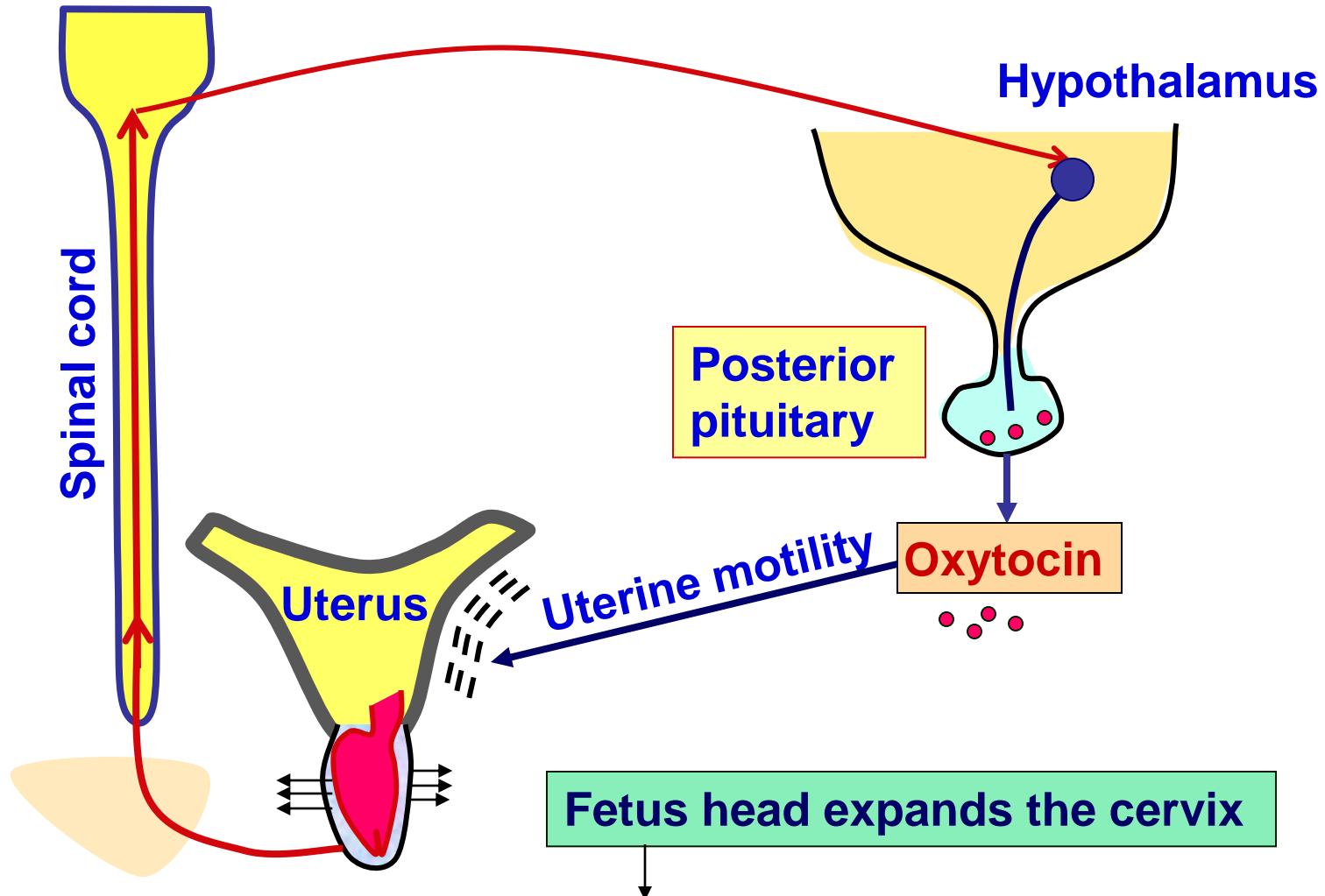




Expulsive stage

Neurohumoral release of oxytocin

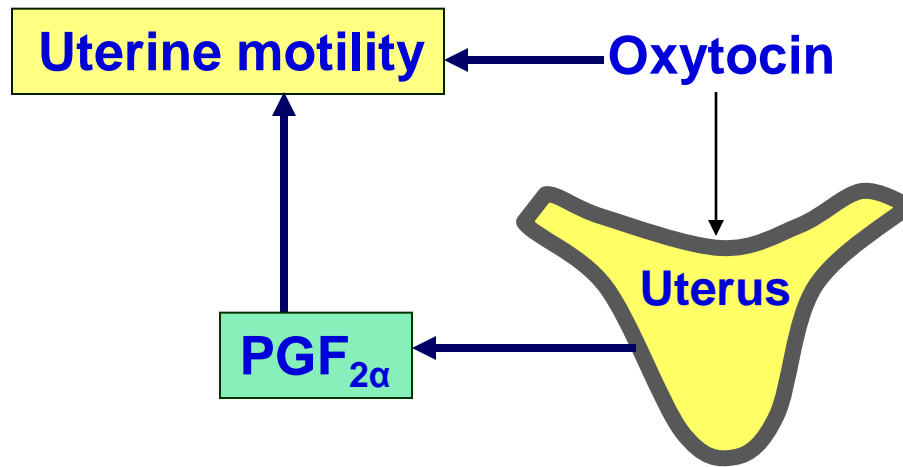
Ferguson reflex



Initiating nerve impulse to hypothalamus

Fetus head expands the cervix

Interaction between oxytocin and PG



Oxytocin

Facilitate release of:

PGF_{2α}

Expulsion of fetal membrane

In liter-bearing animals

Bitch, cat, rat

Immediately after birth

In single bearing animals

Cow, mare, ass, ewe

Few hours after delivery

Purperium

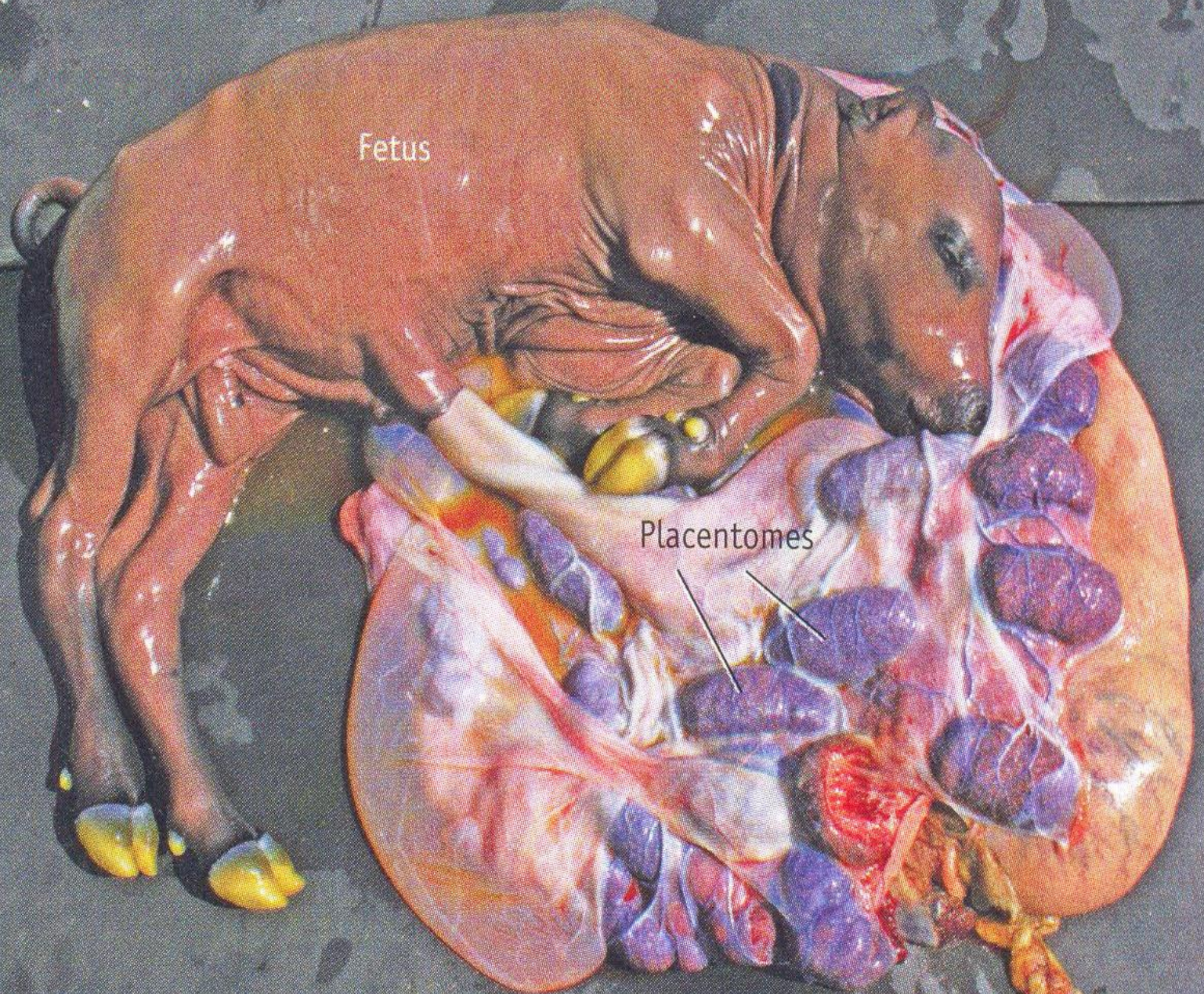
Regain of normal uterine contractility

Expulsion of myometrial fluids

Lochia

Uterus epith. Return to non pregnant state

Uterine involution



Fetus

Placentomes



(a)



(b)



(c)



(d)

Physiology of the fetus and newborn:

Closure of foramen ovale which found between the two auricles to facilitate the oxygenated blood transport from the right side to the left side of the heart without passing through the inactive lung

Closure of the ductus arteriosus that facilitates passage of blood from the pulmonary artery to the aorta

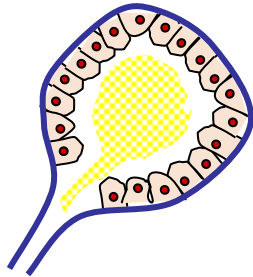
Closure of the ductus venosus that act as hepatic shunt transferring the blood from umbilical vein to the posterior vena cava.

The liver and the kidney are functionally immature

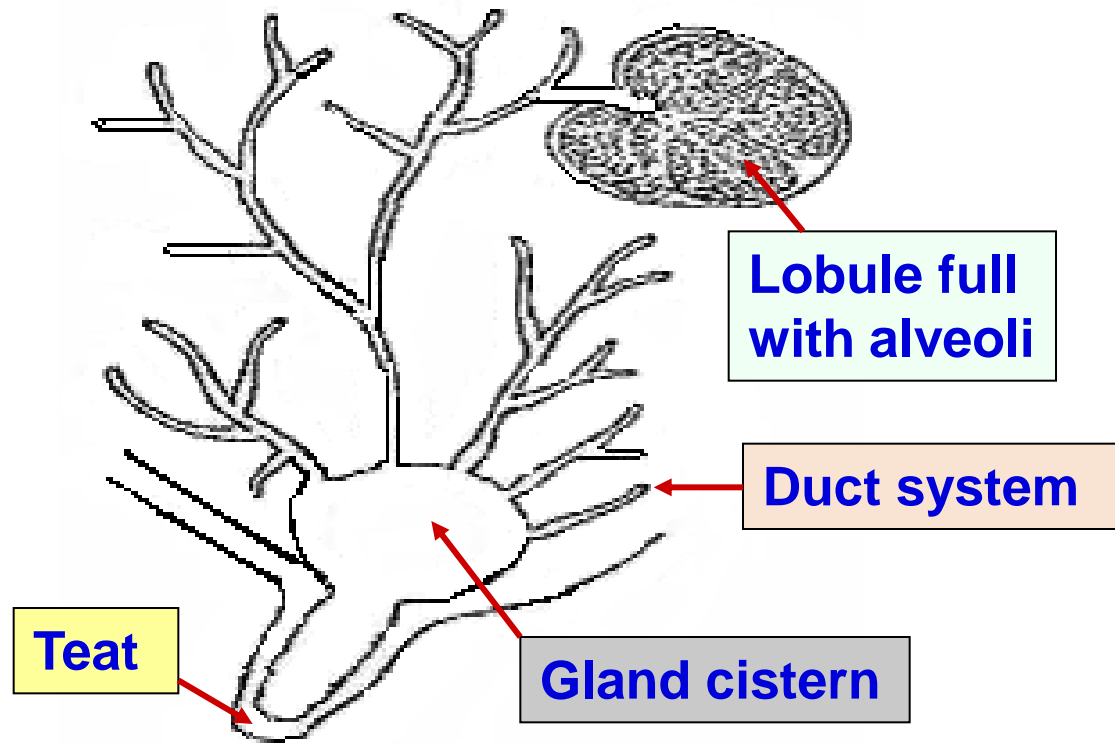
There is a slight jaundiced tint in the skin and eyes of the newborn due to destruction of the excess RBCs and the functional immaturity of the liver.

The intestine contains a dark brown or black tarry material (meconium)

Lactation



Functional unit of the mammary gland



Mammogenesis

Development of mammary gland

During puberty

Estrogen

Begins growth of tubulo-alveolar system

During Reproductive cycles

Estrogen, GH & cortisol

Progesterone & Prolactin

Differentiation of:

Duct system

Alveolar system

During Pregnancy

Mid-gestation

FULL development of the gland

Lactogenesis

**Immunoglobulins
, K, Na, Cl, WBCs,
lactose & fat**

Lactogenesis I

Begins from mid - gestation

**Pre-colostrum
accumulates**

Lactogenesis II

Begins at delivery

Copious milk secretion

**GH, PRL, cortisol,
insulin & PTH**

Blood flow

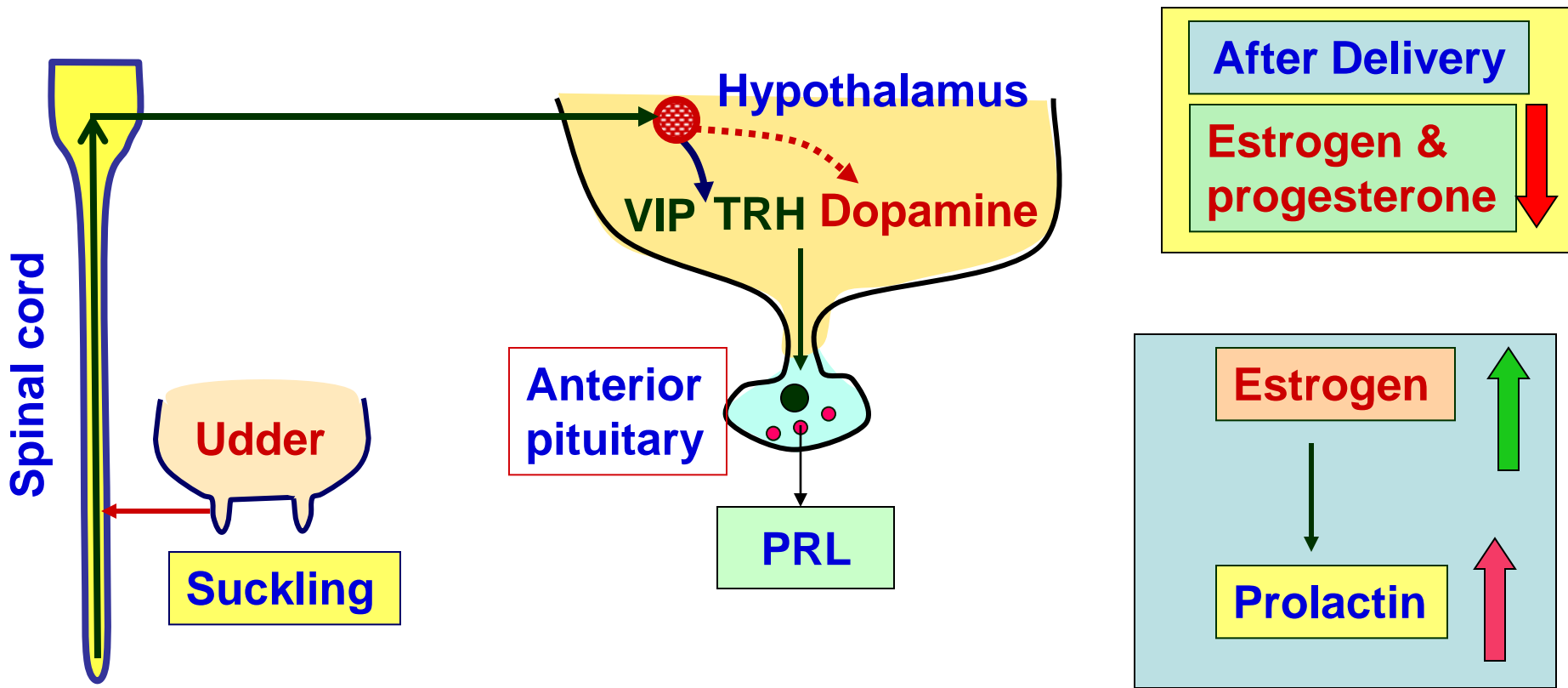
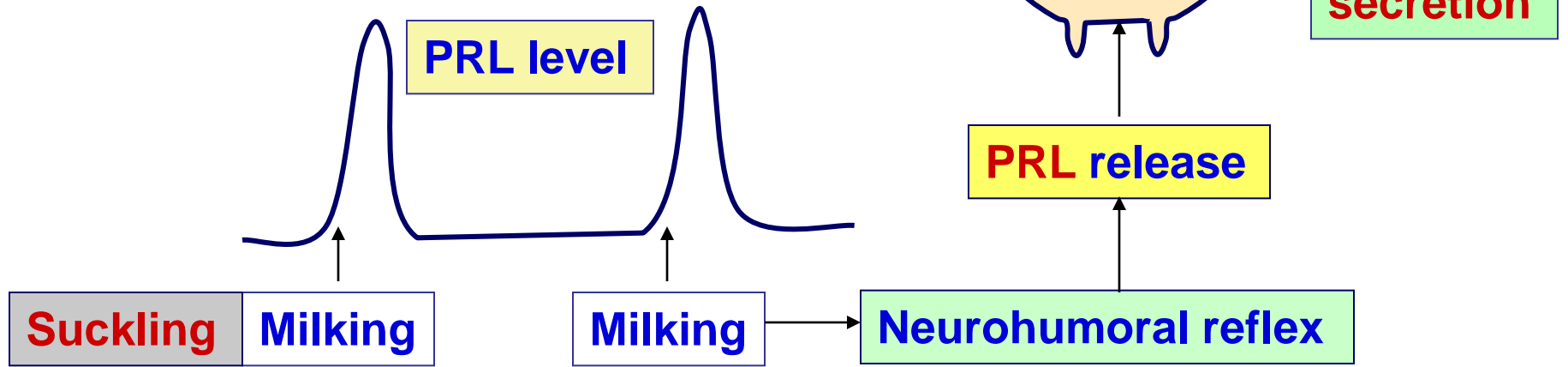
Citrate accumulation

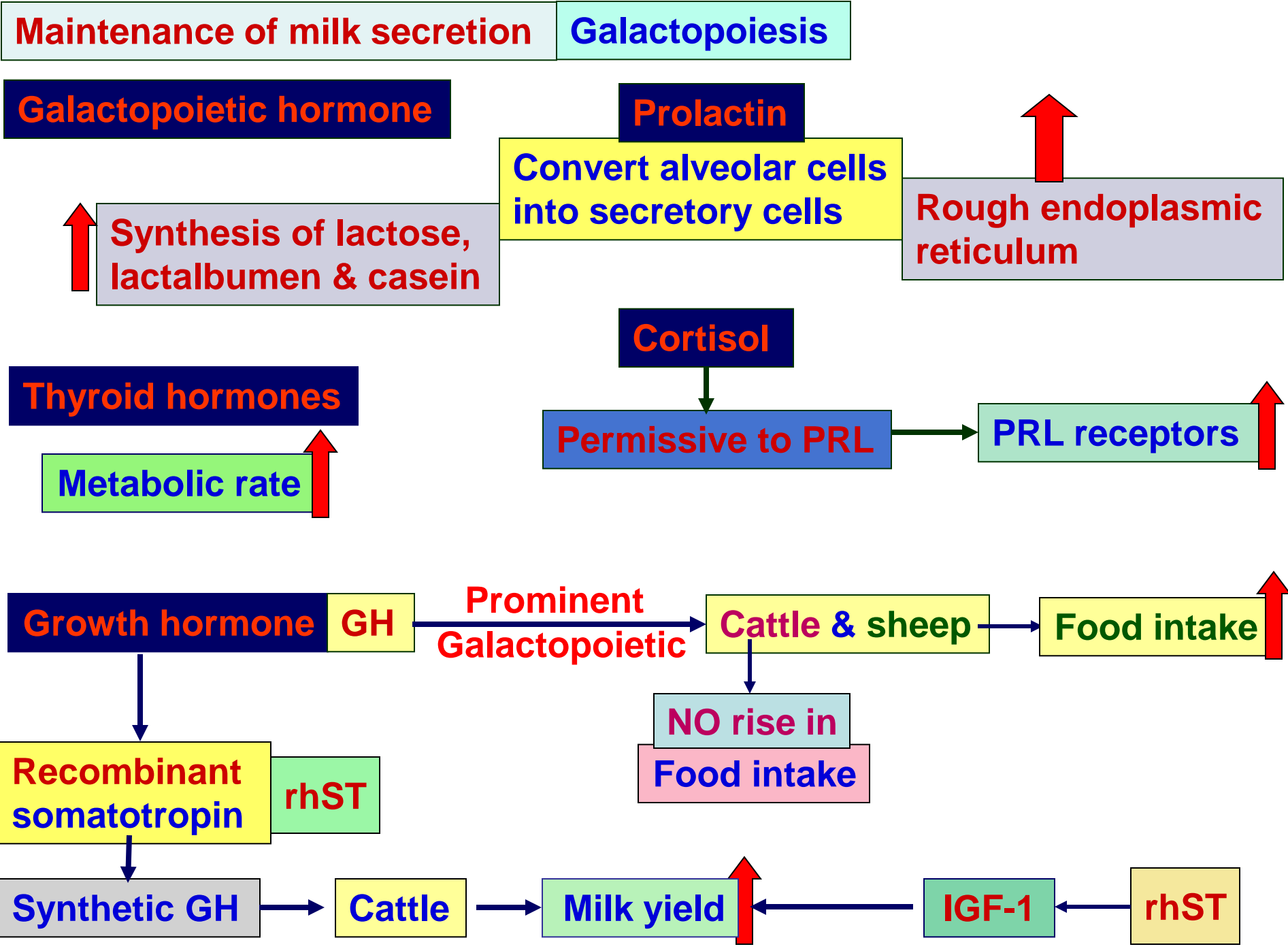
Glucose uptake

O₂ Consumption

Deliver nutrients and elements to the gland

Role of Prolactin (PRL)





Maintenance of milk secretion

Galactopoiesis

Galactopoietic hormone

Prolactin

Convert alveolar cells into secretory cells

Synthesis of lactose, lactalbumen & casein

Rough endoplasmic reticulum

Cortisol

Permissive to PRL

PRL receptors

Thyroid hormones

Metabolic rate

Growth hormone GH

Prominent Galactopoietic

Cattle & sheep

Food intake

NO rise in Food intake

Recombinant somatotropin rhST

Synthetic GH

Cattle

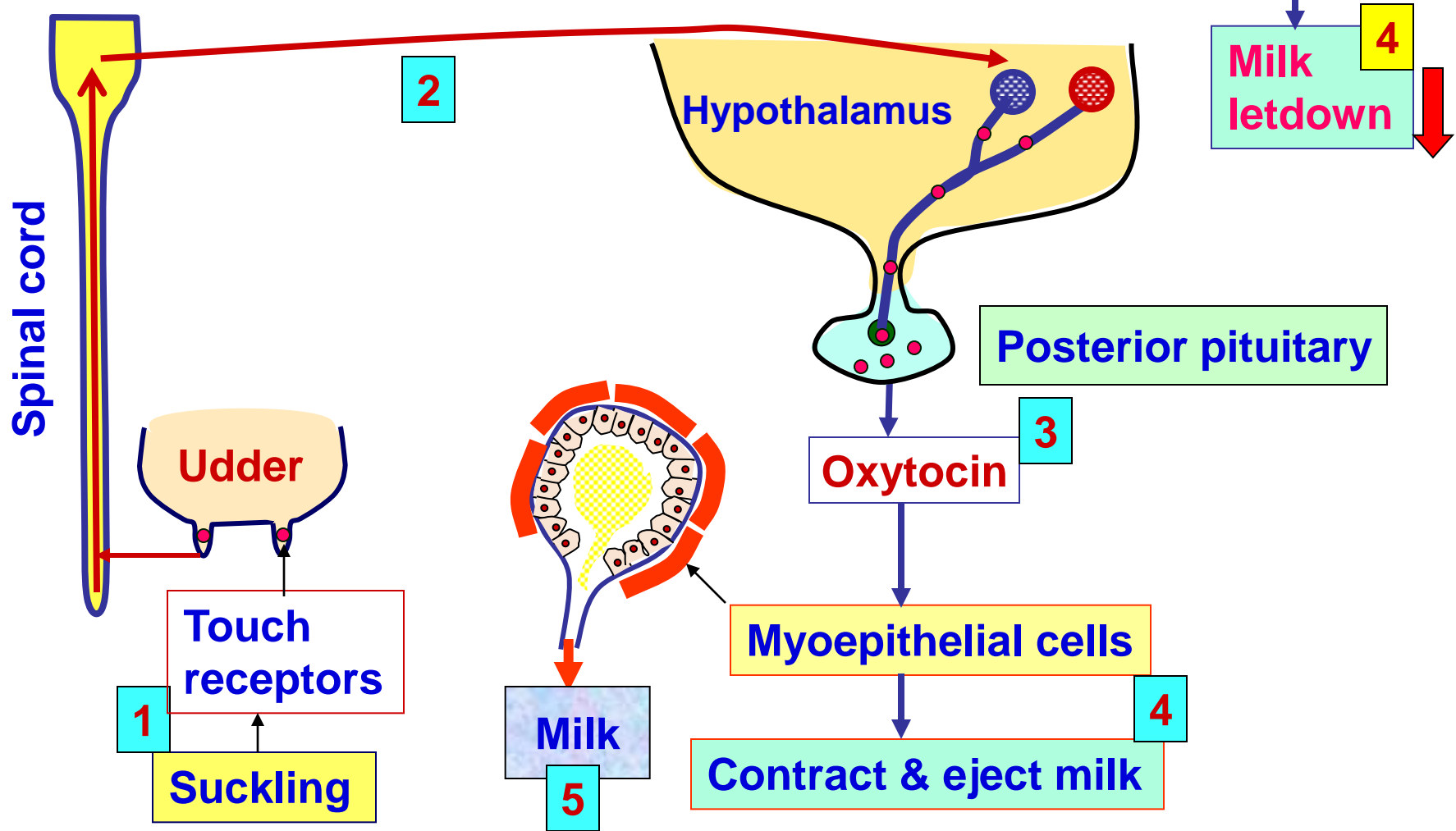
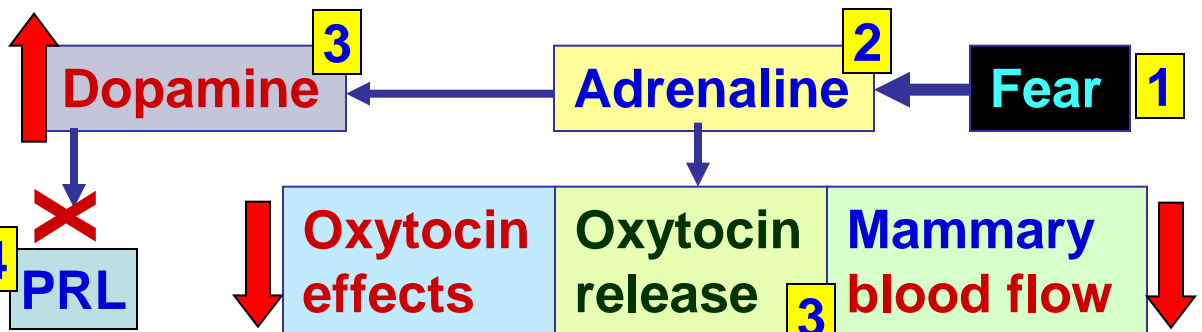
Milk yield

IGF-1

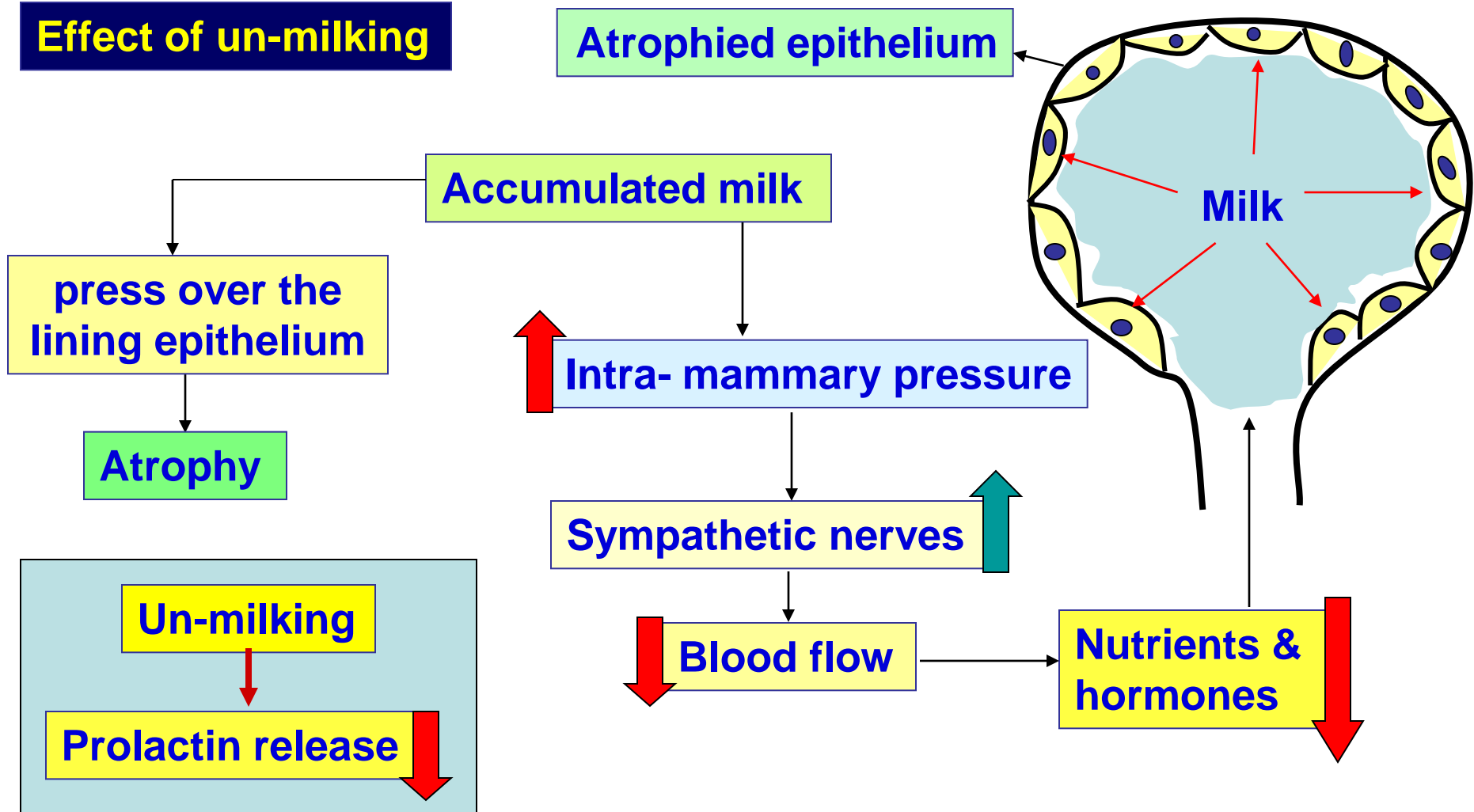
rhST

Milk Ejection

Milk letdown



Effect of un-milking



Colostrum

First milk formed characterized by presence of:

↑ Immunoglobulins

Antimicrobial factors:

↑ Lactoperoxidase

Lysozyme

Lactoferrin

Colostrum is essential for herbivores:

NO immunoglobulin pass through placenta

In primates, bitch, cat & rat

immunoglobulin pass through placenta

Colostrum

Should be consumed directly after birth

Intestinal epith. Is leaky for 24 hours after birth

Pregnant cows shouldn't be transported before delivery

To form Ab against local microbes present

Residual milk

After complete evacuation of the udder

Some milk still trapped in the gland

Can be obtained by:

Oxytocin injection inside the gland











