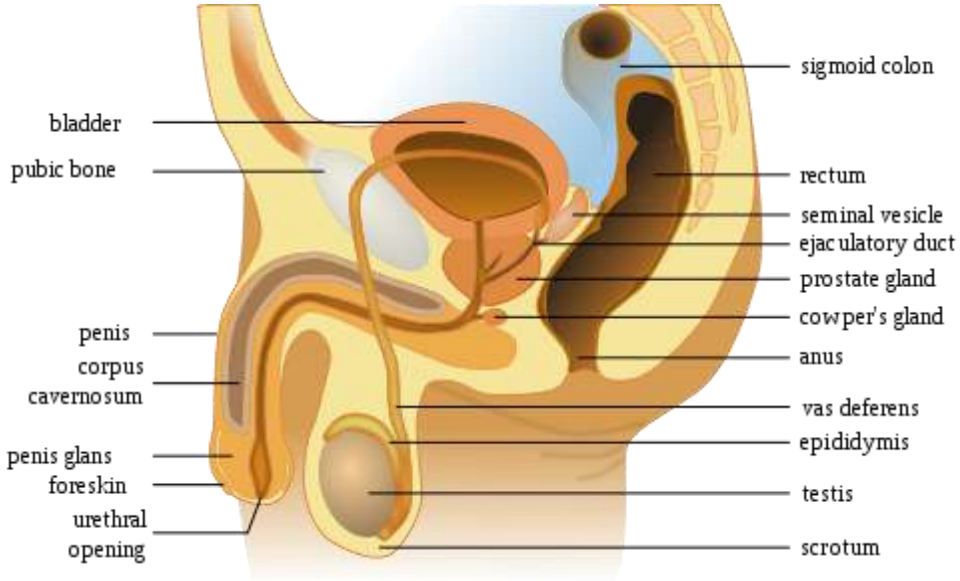
Endocrine Regulation of Male Reproductive Cycle.

Male Reproductive system components.



1. **Two Testes** : that produce sperms and Male sex hormone–Testosterone.
2. **Accessory glands**:

   (Prostate Gland, Seminal vesicles, Bulbo urethral gland etc.)

   Secrete fluid for carrying sperms to penis

   Fluid + Sperms = Semen
3. **Accessory ducts** : that store and carry secretions of testes and accessory glands to penis.

   (Epididymies, vas deferens, ejaculatory duct etc.)
4. **A penis** : that deposits semen in the vagina during sexual intercourse.

For maturation and normal sexual function, hormones, regulatory hormones are must.

Male sex hormones are collectively known as Androgens (Gr. andros – man, gennan - to produce)

Hormones that travel from brain (Hypothalmus) to pituitary and from pituitary to testes are known as "Gonadotropins"

The control of male reproductive cycle (functions) by hormones is illustrated by Fig. 1.

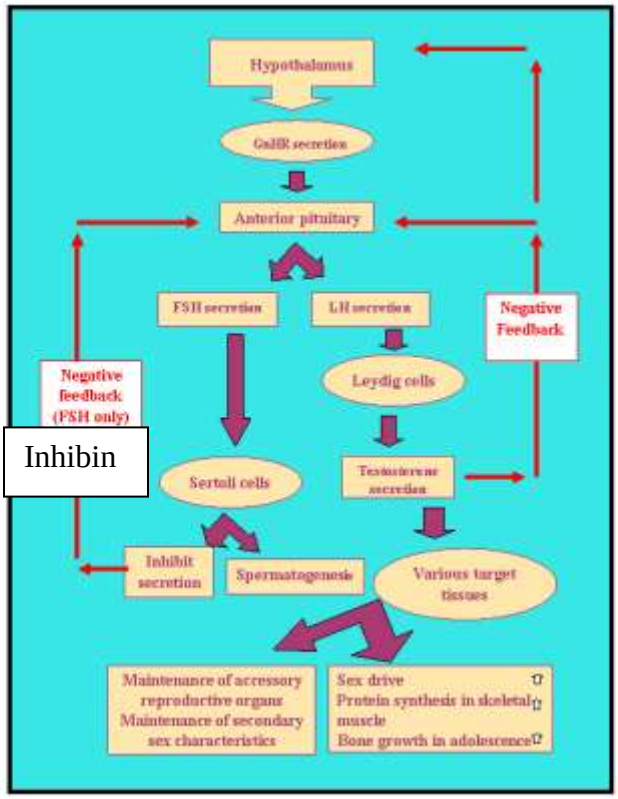
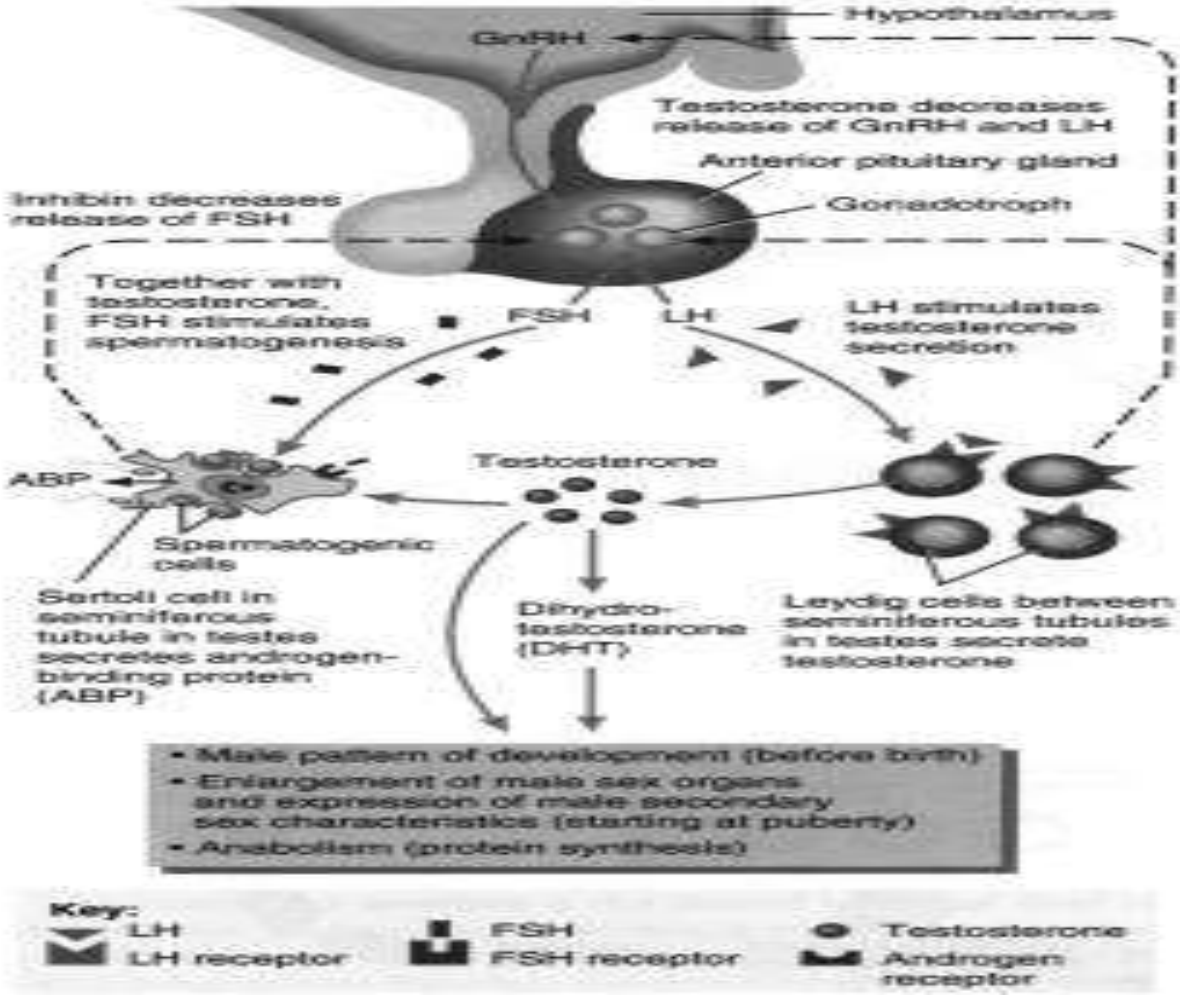


Fig. 1 Harmonal regulation of male reproductive function.



As shown in the fig. 1, GnRH (Gonadotropin releasing hormone) regulates release of Gonadotropins (LH & FSH). Pituitary secretes Luetinizing Hormone and Follicle Stimulating Hormone (LH & FSH). LH (ICSH – Interstitial cells stimulating hormone) stimulates interstitial cells (Cells between the seminiferous tubules) of testes to secret testosterone (This has negative feedback effect on secretion of LH). It performs various functions such as development of primary and secondary sex characters, spermatogenesis, muscle development, behavioural changes etc.

FSH stimulates spermatogenic cells in testes to produce sperms. With its sufficient titre the spermatogenic cells secrete a substance inhibin which inhibits secretion of FSH.

Testosterone and other male sex harmones (Androgens)

1. Leydig's cells secrete the hormone testosterone. In target tissues it gets converted to more active form dihydrotestosterone and to some extent to androstenedione.
2. Adrenal glands secrete 5 different Androgens but their quantity is negligible both in males and females. They mainly affect dev. Of public hair and axillary hair.
3. Sertoli cells in tests produce small quantity of Estrogens. ($1/5^{th}$ of non pregnant females). Their exact function in males is not known.

Functions of testosterones.

- Mainly responsible for developing masculine characters.
- Testosterone is produced for a few weeks after birth. Then no testosterone till age 10 to 13 years. Then it increases under the stimulus of gonadotropic hormone from anterior pituitary.
- Testosterone secreted by developing genital ridge or tests causes development of male genitals such as penis, scrotal sacs, prostate gland, seminal vesicles and suppresses development of the female genital organs.
- Testosterone secreted after puberty causes almost 8 fold growth of genitals and development of secondary sexual characters.

Body hair : over pubis, umbilicus and above, on chest, face, sometimes on back.

Voice : Testosterone causes hypertrophy of laryngeal mucosa, enlargement of Larynx and hence cracking of voice. This changes to typical masculine bass voice.

Effect of skin: Testosterone increases thickness of skin over the entire body and increases ruggedness of subcutaneous tissue. It increases rate of secretion of some sebaceous glands especially of face. Their over secretion can result in acne, which is important feature of adolescence. As years pass, the skin adapts to testosterone levels to overcome acne.

Protein Formation and Muscular development:

After puberty testosterone causes almost – doubling of muscle mass which is associated with increase in protein formation. Changes in skin and voice are also related to excess protein deposition. Due to this property the athelets use testosterone for muscle development. In old age also testosterone is used to maintain strength and vigor.

Effect on Bone and calcium retension:

After puberty or by testosterone injection, the bones grow considerably in thickness, there is significant dipositon of calcium salts.

It has significant effect on Pelvis. It lengthens it; causes its funnel shape instead of broad ovoid shape of female pelvis. The increased length increases strength of bearing load.

As testosterone increases strength of bones it is used in old age to prevent osteoporosis.

Effect on Basal Metalolism :

During active sexual life testosterone increases Basal Metabolic Rate (BMR) by 5 to 10%. This is mainly due to its effect of protein anabolism.

Effect on RBC :

Testosterone gives more number of RBC (about 700,000/mm^3) in males than a females. This is probably due to increased BMR.

Abnormalities of male sexual function.

1. Prostate gland :

Prostate is small in child hood.

Normal size in age 20 to 50.

After 50 begins to degenerate due to low Testosterone secretion.

- In some benign fibroadenoma of Prostate develops. This causes urinary obstruction.
- Prostate cancer grows rapidly. Spreads in bones also causing severe bone pain. It can lead to death. For treatment, testes are removed (to prevent testosterone secretion) or female hormone estrogen in given (or both)

Hypogonadism

Reasons : (i) Birth without functional testes (2) Under developed Testes due to failed secretion of Anterior pituitary.
(3) Undescended testes – Cryptorchidism – causing total or partial degeneration of testes. (4) Genetic absence of androgen receptors (rare). (5) Loss of testes – castration.

In case of (1) & (2) instead of male sexual organs female organs are formed. In case of (3) voice child like, secondary sexual characters like child, Avg. height slightly more than normal individuals.

In case of (5) there is reversion of sexual characters.

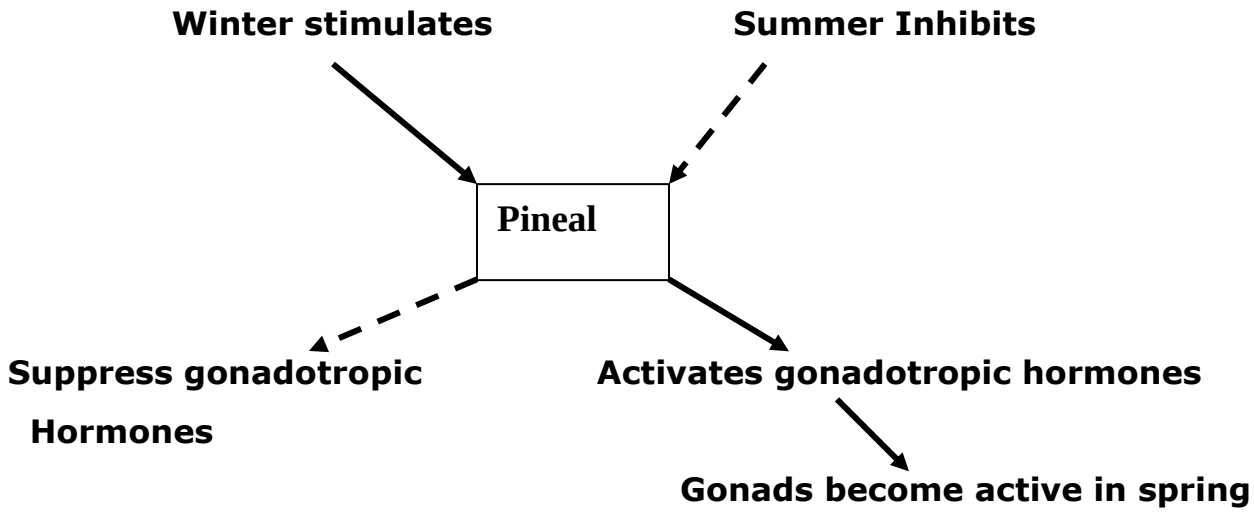
Hypergonadism

Sometimes Interstitial Leydig's cell tumor develops. This increases testosterone 100 times that of normal. This leads to rapid growth of musculature and bones. But height of adult is actually less than normal individuals. The sexual organs and secondary sexual characters are more developed.

Pineal gland

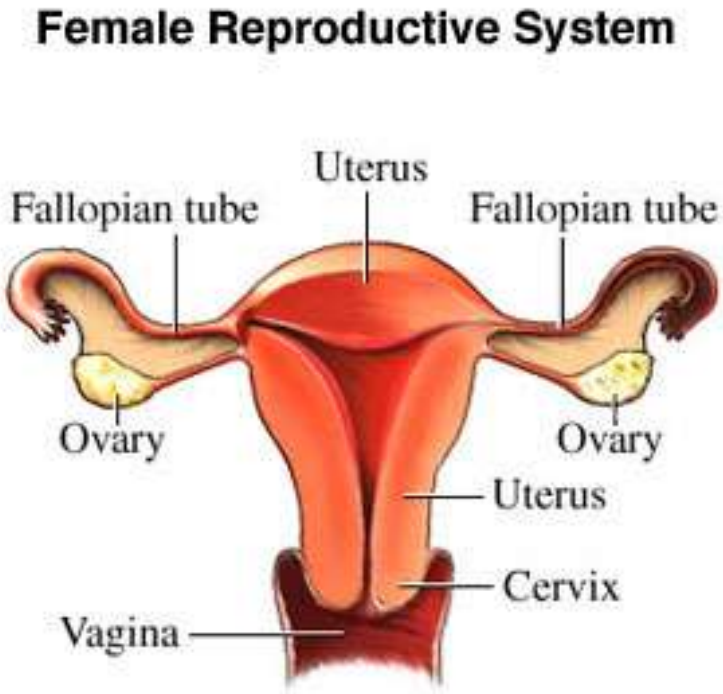
Secretions are known to suppress secretion of glandotropic hormones. Due to this reason the pineal tumors affect the sexual characters adversely. In lower animals, winter season with shorter day time, stimulates pineal hence suppresses the gonads. The gonads however become active in spring / summer.

In Lower animals



Endocrine regulation of female Reproductive system :

Female reproductive system – Components



1. **Two ovaries** : produce eggs and female sex hormones estrogen and progesterone.
2. **Two Uterine tubes** : One from each ovary carry eggs from ovary to uterus. Fertilization usually occurs in upper $1/3^{rd}$ part of uterine tubes.
3. **Uterus** : Receives the blastocyst (formed after fertilization and houses developing embryo.)
4. **Vagina** : Receives semen from male Penis during sexual intercourse. It is exit point for menstrual flow, also a canal through which baby passes at the time of birth.
5. **External Genital organs** : have protective function and play role in sexual arousal.
6. **Mammary glands** : Provide milk to newborn baby. They are modified sweat glands.

Endocrine regulation of female reproductive cycle.

The female reproductive cycle begins on attaining puberty. Males are continuously fertile from puberty to old age and sex hormones are secreted through out that period. In female, on reaching puberty, she is fertile only during a few days each month. The patterns of hormonal secretion are complicated and cyclical.

The main reproductive cycle has two important events.

1. Maturation of ovarian follicle, Ovulation, Formation of corpus luteum, regression of corpus luteum.
2. Development of uterine wall (endometrium) for implantation of embryo and sloughing of the endometrium (absent in some animals) i.e. menstruation if implantation does not occur.

Following two figures show hormonal control of the reproductive cycle.

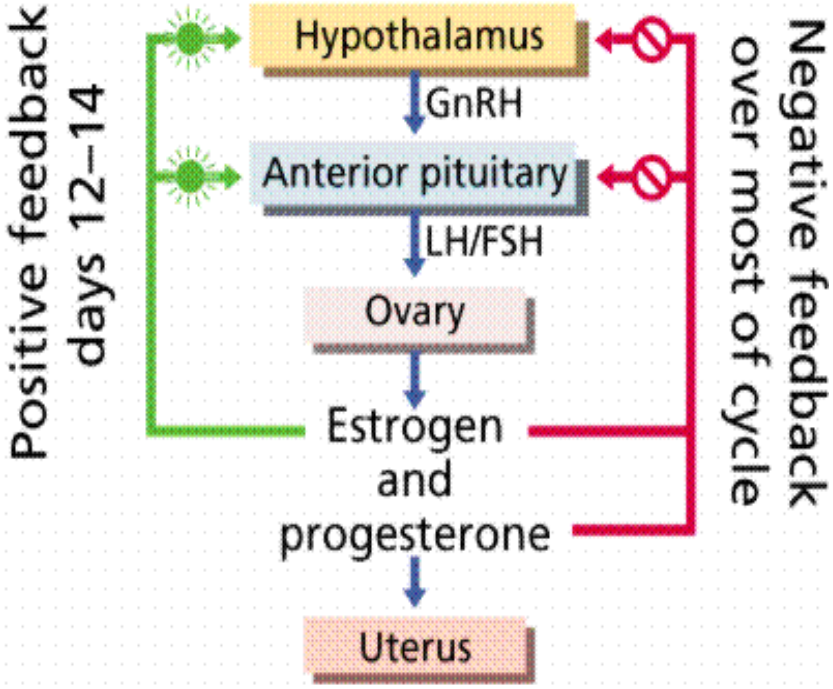


Fig. 1 Hormonal control of reproductive cycle of adult female (mammals mainly)

As shown in fig 1. Hypothalamus stimulates Anterior pituitary through GnRH (Gonadotropin Releasing Hormone). Anterior pituitary secretes FSH & LH (Follicle Stimulating Hormone and Luteinizing Hormone). Both govern maturation of follicle in the ovary. The follicle secretes Estrogen which is responsible for development of secondary sex characteristics of female. It also stimulates growth and thickening of endometrium of uterus.

Estrogen initially gives positive feedback to hypothalamus giving an initial surge of LH only. Later on when proper FSH & LH level is reached estrogen has negative feed back effect of Anterior pituitary. This keeps hormonal level balance.

After ovulation the follicle becomes Corpus Luteum which secretes progesterone (and some estrogen). This governs maintenance of Endometrium for possible implantation.

The events in ovarian and Menstrual cycle are shown in fig. 2 which also shows plasma hormonal level changes in FSH, LH, Estrogen and Progesterone.

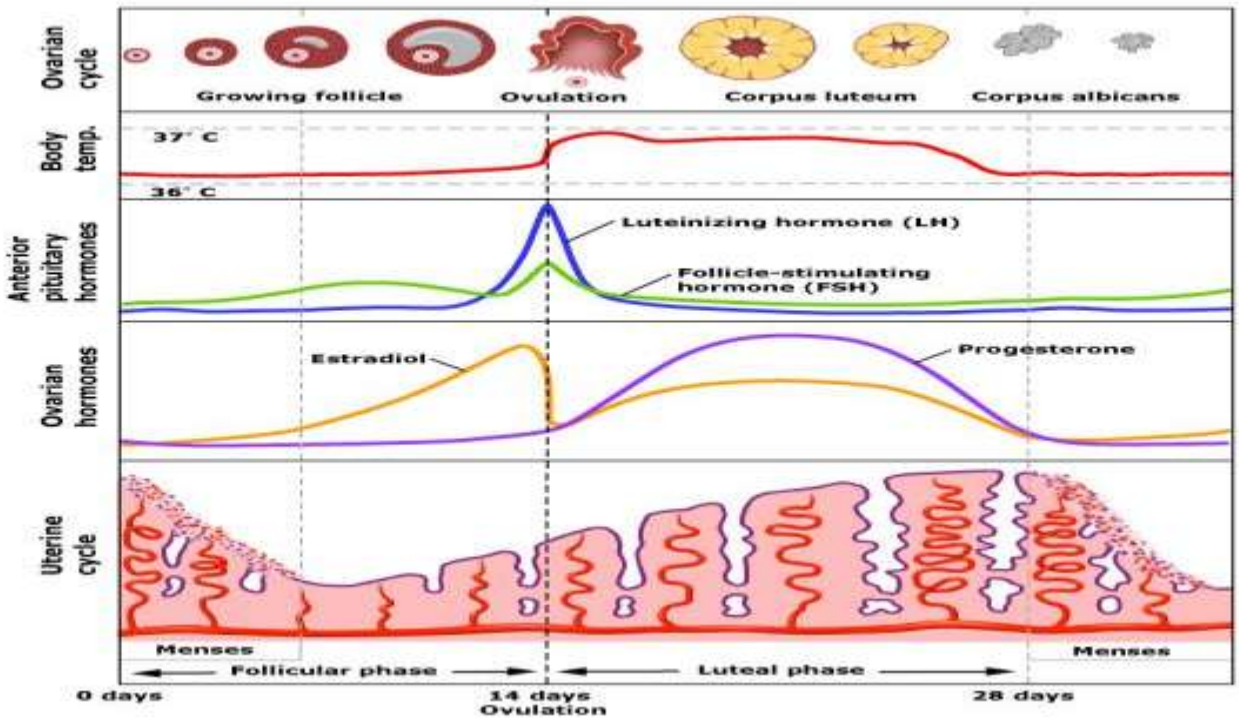


Fig.2.- Menstrual Cycle in human female.

In case the fertilized ovum gets implanted in the uterus there are further events like pregnancy, parturition (birth), milk production (Lactation) which are also hormonally governed.

Following table summarizes the functions and source of different hormones governing female reproduction. (Refer Table)

Table : Major Human female Reproductive Hormones.

Sr. No.	Hormone	Functions	Source
1.	Estrogen	Stimulates thickening of uterine wall, Maturation of oocyte and development of female sexual characters. Increases LH Inhibits FSH Secretion.	Ovarian Follicle and Corpus Luteum.
2.	FSH (Follicle	Development of oocyte and	Pituitary gland

	Stimulating Hormone)	follicle. Increases Estrogen secretion, stimulates new gamete formation and development of Uterine wall after Menstruation.	
3.	GnRH (Ganadotropin Releasing Hormone)	Controls secretion of LH and FSH by Pituitary.	Hypothalamus.
4.	LH (Luteinizing Hormone)	Stimulates further dev. Of oocyte and follicle, stimulates ovulation, increases proges-terone secretion, aids in development Of Corpus Luteum.	Pituitary gland
5.	Oxytocin	Stimulates uterine constractions during child birth. Also milk ejection during nursing.	Pituitary (Posterior) Neurohypophysis
6.	Prolactin	Promotes milk secretion by mammary glands after child birth.	Pituitary Adenohypophysis
7.	Progesterone	Stimulates thickening of uterine wall.	Corpus luteum.

In lower vertebrate groups also the gonadal development and reproductive cycle are regulated by secretions of pituitary. The gonadal fertile period may be seasonal, once in year, twice in year or continuous cyclical. In fish and Amphibia fertilization is external. In reptiles and birds it is internal and after fertilization there is yolk deposition and egg shell formation.

As shown above apart from the female cycle regulating hormones GnRH, LH, FSH, Estrogen, Progesteron the other two Oxytocin and Prolactin play important role in the events child birth, milk secretion and nursing.

OESTRUS

Estrus (Gr. Oistros, a vehement desire) cycle – (Heat) :

Most mammals have a definite time or times during the year in which ova (eggs) mature and are capable of being fertilized. Reproduction usually occurs when climatic conditions and resource characteristics favour successful development. Certain mammals like man, who maintain goods constancy of internal environment or those who are living in environments with few seasonal changes may reproduce any time in the year. However, they are still tied to physiological cycles of the female, that determine when ova can be fertilized.

Most female mammals undergo **ESTRUS CYCLE** which includes a time during which the female is behaviourally and physiologically receptive to male.

During the Estrus the hormonal changes stimulate maturation of ova in ovary, induce ovulation (release of one or more mature ova from the ovarian follicle). After or around ovulation the females are receptive to the mating with male. (In a few mammals like rabbits ferrets and minks the copulation induces ovulation.)

As shown in the diagram ahead, the hormones govern the changes in the ovaries and also uterus. As the ova are maturing the inner lining of uterus proliferates and becomes more vascular. This is for receiving the embryo. This is also associated with external swelling in the vaginal area, increased glandular discharge and proliferation of vaginal mucosa. During this time male shows more interest in female and females are more receptive to males.

If fertilization does not occur, the changes in the uterus and vagina are reversed until the next cycle begins.

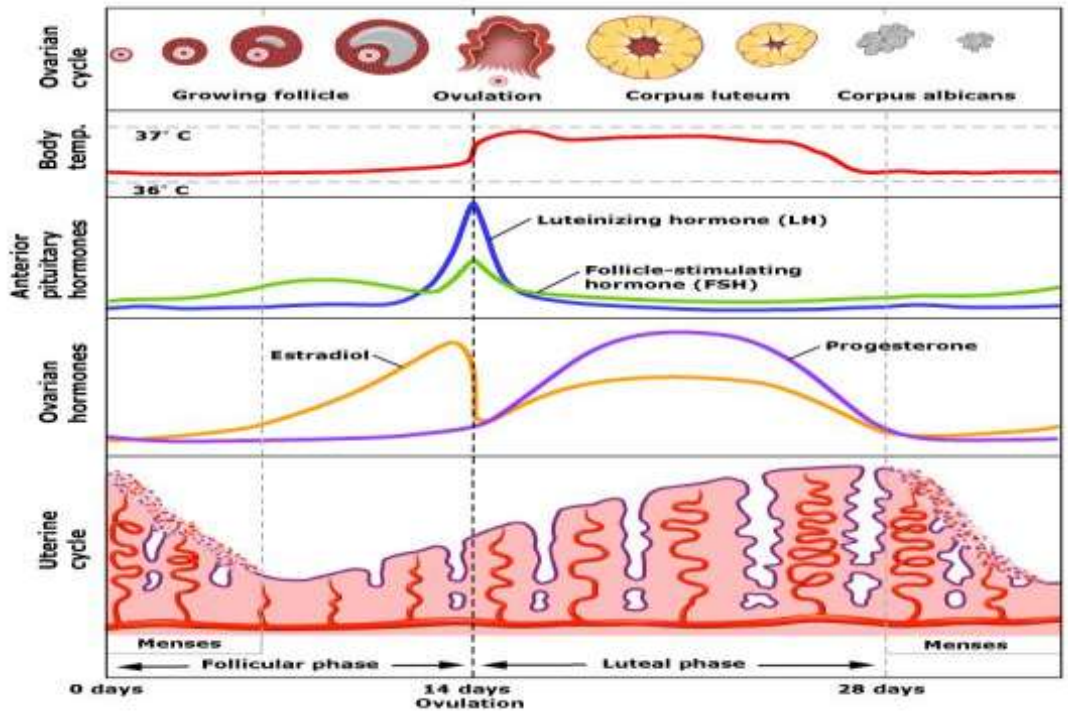


Fig. 1. Hormonal regulation of ovarian and uterine events during Estrus Cycle / Menstrual cycle.

- Many mammals are monestrous – Single yearly estrus cycle. e.g. Wild dogs, Bears, Sea Lions.
- Domestic dog are **DI-ESTRUS**. (2 cycles per year)
- Many mammals are **POLY-ESTRUS**. Many cycles per year. e.g. In rats and mice estrus cycle is repeated every 4^{th} to 6^{th} days.

In Human, Apes, Monkey females– ♀ If fertilization does not occur before the end of estrus cycle there occurs sloughing of uterine lining – **Menses**. Hence the cycle is known as **Menstrual cycle.**

Following table shows events in ovaries and vaginal histology (studied by vaginal smear) in rat estrus cycle.

The stages are --

Diestrus or Anestrus – No estrus : uterine wall not thickened.

Pro estrus : Beginning of Estrus changes.

Early estrus: Thickening of Endometrium starts

Late estrus: Thickening of Endometrium fully formed.

Metestrus: Cornified vaginal epithelium begins to break down.

Anestrus / diestrus begins.

Table 1 : Events in ovaries and vaginal histology of rate during estrous cycle.

No.	Name of Stage	Duration of Stage	Ovarian Events	Types of cells in vaginal smear
1.	Di estrus or An estrus	Half of whole cycle	Corpora lutea degenerated	Nucleated Epithelium and leucocycles.
2.	Pro estrus	12 hrs	Follicles growing fast (mating occurs at this time)	Nucleated Epithelal cells
3.	Early Estrus	12 hrs.	Follicles growing fast (mating occurs at this time)	Cornified cells
4.	Late Estrus	18 hrs.	Ovulation Occurs	Cornified cells.
5.	Metestrus	6 hrs.	Corpora Lutea formed	Leucocytes among cornfied cells
6.	Beginning of Diestrus		Functional Corpora Lutea during early part.	Cornified cells disappearing.

The length of Estrous cycle, duruation of heat and time of ovulation differs from animal to animal. Following table gives a few examples.

No.	Animal Name	Length of cycle days	Duration of Heat	Time of ovulation.
1.	Woman	28	Continuous	12 to 15 days of cycle.
2.	Cow	21	13 to 17 Hours	12 to 15 hrs after heat.
3.	Mouse	4	10 hrs.	2 to 3 hrs after start of heat.
4.	Dogs	yearly 2 heats	7 – 9 days	1 to 3 days after start of heat.

Menstrual Cycle.

The Menstrual cycle is observed in (Primates), Female humans, Apes, Monkey. It is similar to estrus cycle in that it results in periodic proliferation of inner lining of the Uterus and correlates with maturation of an ovum. However if

fertilization does not occur before the end of the cycle, menses – the sloughing of Uterine lining – occurs.

Please Note :

- Give Fig. 2 from notes Endocrine regulation of female reproductive system.
- Below the figure explain role of FSH in stimulating follicle growth and ovulation. Role of LH in stimulating progesterone and Estrogen secretion from corpus luteum. How the two regulate dev. Of endometrium in Uterus. How if fertilization does not occur there is sloughing / menses / menstruation.

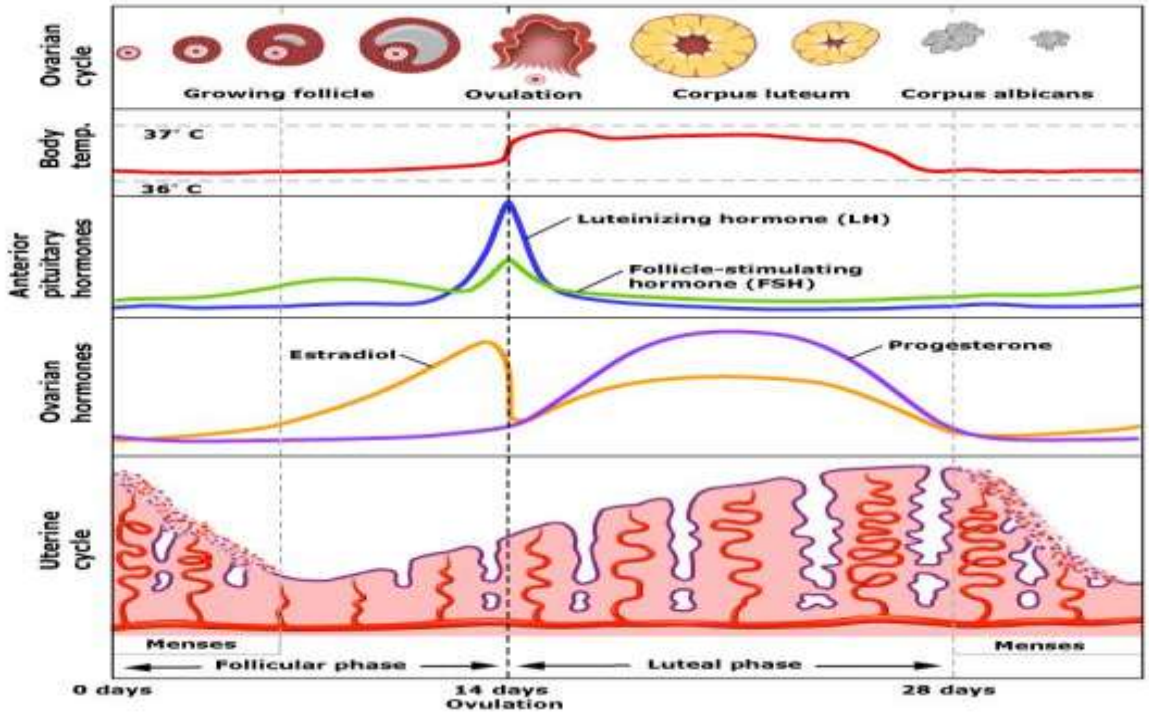


Fig.2.- Menstrual Cycle in human female.

Then add the following-

It has been experimentally proved in case of Primates that (1) removal of ovaries causes menses (bleeding) (2) Sloughing off (menses) can be prevented by either estrogen or progesterone. However presence of progesterone is more significant. Decline in progesterone leads to menses. As shown in following

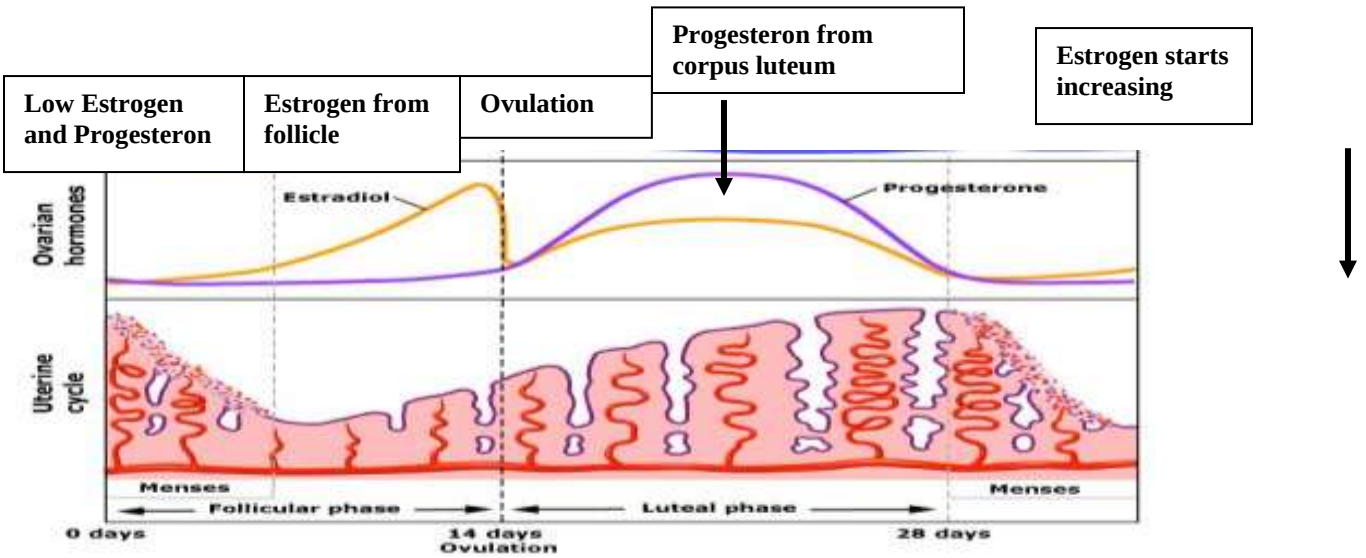
figure menses occurs when both Estrogen and Progesterone are low. After 2 - 3 days menses stop because estrogen slowly increases in quantity.

Box 1

Maintenance of C. Luteum is governed by various things.

- In Rats, Mice stimulation of cervix (by copulation or artificial) passes nerve impulses to hypothalamus. Through Anterior pituitary it regulates secretion of LH to maintain Corpora Lutea.
- Nerve impulses from uterus also are important. If beads are implanted in the uterus they cause transmission of nerve impulses to hypothalamus / pituitary to cause release of LH and hence maintenance of Corpora Lutea.
- In both the above cases neural links between cervix/Uterus and pituitary have been established.

Fig. Relation of Hormonal state to Menstruation.

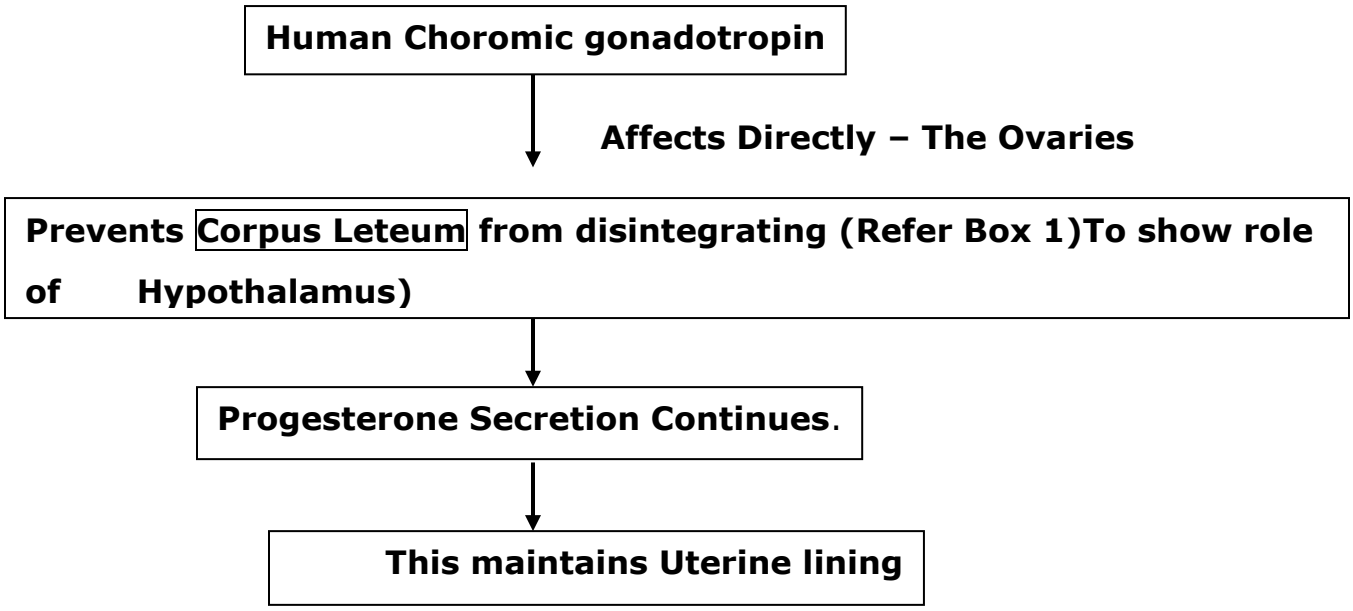


Comparison of Estrous and Menstrual cycle.

Estrous cycle	**Menstrual cycle**
1. Observed in Non primates	1. Observed in Primates.
2. Physiological and Marphological changes in the ovaries, vagina, uterus are identical in both.	2. Physiological and Marphological changes in the ovaries, vagina, uterus are identical in both.
3. Periodic peaks of sexual receptivity (heat). Once in a year (Mon-estrus) or twice in a year (di-estrus) or many times in a year. (Polyestrus)	3. Sexual receptivity through out.
4. Sloughing of uterine Endometrium / Menstrual bleeding not seen.	4. Sloughing of Uterine Endometrium / Menstrual bleeding occurs / if fertilization does not take place.
5. In Non – primates pseudomenst-ruation is seen usually due to very high hormone Estrogen.	5. Menstruation in primates is due to absence of hormones (mainly progesterone.

Pregnancy (Mammals) : In human

Pregnancy sets into motion a new series of physiological events. As the embryo develops the cells of embryo and placenta release hCG.



After some period Placenta takes over the Progesterone secretion and corpus luteum degenerates (Refer Box 2)

In 3rd week of pregnancy the hCG in blood increases so much that it is excreted in urine. It can be tested immunologically in the urine. (this is the Pregnancy test)

Box 1

Maintenance of corpus luteum is governed by various things.

- **In rats, mice stimulation of cervix (by copulation or artificial) passes nerve impulse to hypothalamus. Through Anterior pituitary it regulates secretion of LH to maintain Corpora lutea.**
- **Nerve impulses from the uterus also are important. If beads are implanted in the uterus they cause transmission of nerve impulse to hypothalamus/ pituitary to cause release of LH and hence maintenance of corpora lutea.**
- **In both the above cases neural links have been established.**

Box 2

As mentioned above the Corpora lutea in the ovary are the source of progesterone in the beginning of pregnancy. Later on placenta becomes the source. However the situation varies from animal to animal.

- **In Rats ovaries are essential throughout pregnancy (gestation)**
- **In Opossum, Hamster, Mouse, Rabbit, Goat, Gr. Squirrel ovaries are essential throughout pregnancy (gestation) In them castration (Removing ovaries) causes Abortion or failure to implant.**
- **In cow ovary is not necessary after 7 month pregnancy.**
- **Ewe, Bitch, Mare, Cat, Guinea Pig, Monkey, Women do not abort if ovaries are removed in 2nd half of pregnancy. This is because function of C. Luteum is taken over by placenta.**

Pregnancy in Woman has following main events.

1st Trimester – (3 months)

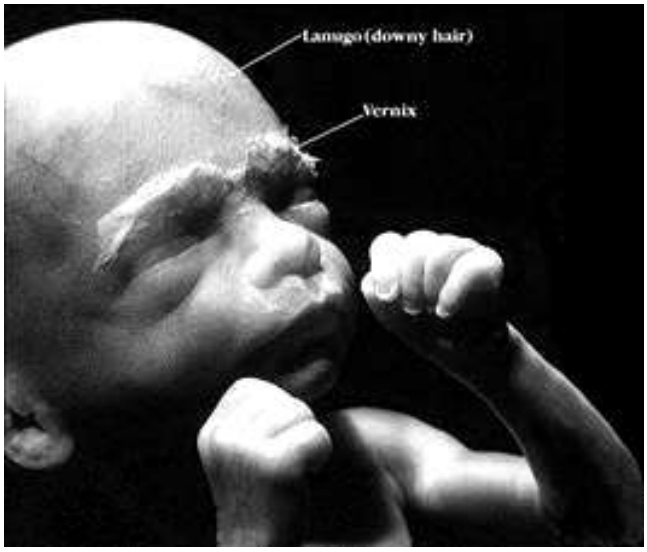
- Fertilization occurs in upper 1/3rd of Uterine tube.
- Implantation of Blastocyst (Trophoblast)
  11 to 12 days from fertilization
- By 45 days major body systems start developing.

The embryo at six weeks

The fetus at 14 weeks

2nd Trimester

- Fetal movements can be felt in 4th month.
- Heart beats can be heard.
- Upper and lower eyelids separate, Eyelashes form (6 month).
- Bones begin to ossify.

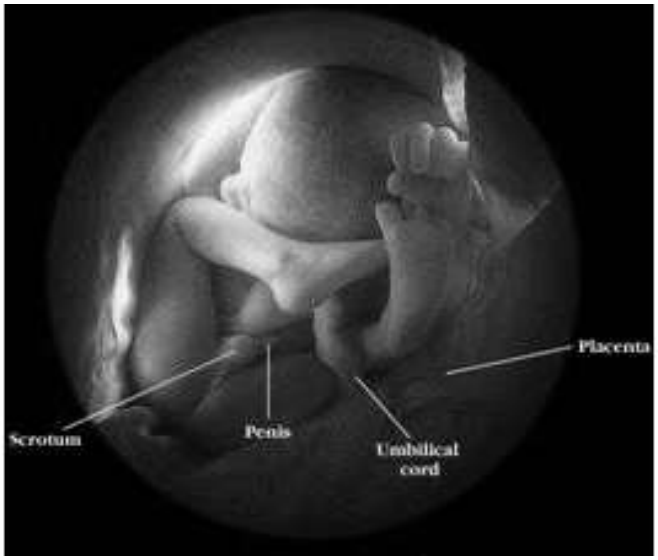


The fetus at 24 weeks

3rd Trimester –

- 7 month – Eyes open
- Circulatory and respiratory system well formed.

  ∴ Child can survive if borne prematurely.
- In last month fetal weight doubles.



The fetus at 32 weeks

During pregnancy The placenta is the hormone producer as well as it is exchange site.

Of the embryonic membranes amnion, chorion and allantois, the Chorion and allantois give rise to embryonic part of placenta. In placenta there are numerous Chorionic Villi which contain blood vessels from the mother. In close contact with these vessels there are blood vessels from fetus. Gases and nutrients are exchanged here (The bloods of fetus and the mother actually do not mix with each other; there is only exchange of nutrients). The major blood vessels coming from and going to the fetus are 2 arteries and a vein. They are in the Umbilicus. The umbilical vein carries nutrients and oxygen to the fetus. The 2 Umbilical arteries bring deoxygenated and nutrient depleted blood to placenta.

Birth : Parturition (L. parturire, to be in labor)

In human the child birth occurs after 266 days from fertilization or 280 days from the beginning of last menstrual period. When it is time for the baby to be born following things occur.

Pituitary of Baby secretes
Adrencorticotropic Hormone ACTH

↓

Stimulates Adrenal Glands (of baby) to secrete Steroids.

↓

Stimulate Placenta to produce Prostaglandins

↓

And oxytocin from Mother's Pituitory

↓

Cause Powerful contractions in Uterus Muscles.

↓

They further stimulate oxytocin production to increase strength and length of contractions. The contractions last 2 to 18 hrs.

↓

During this time the Cervix becomes fully dilated
Amniotic sac ruptures. Ovaries and placenta secrete Hormone Relaxin

↓

Cause slight separation of Pelvic Bones so that baby can pass through the birth canal. Also cause dilatation of cervix.

- Usually the baby is expelled from uterus within 1 hour.

- After the baby is born uterine contractions continue to expel the after birth remains.

In Human the unbilical cord is served (cut) with some instrument. In other mammals the female bites through the cord to sever it.

During birth process the baby (fetus) suffers lot of stress when it passes through birth canal. The stress is in form of pressure, deprivation of oxygen for some time.

Stress

↓

Stimulates Secretion of Epinephrine and Norepinephrine (Catecholamines) by Adrenal of fetus. (Fetal Adrenal glands are relatively big as compared to adult).

↓

These stress Hormones help the fetus.

- To over come the extreme stress.
- To adjust to new conditions outside mother's uterus.
- These postnatal (after birth) adjustments include
  1. Breathing
  2. Breaking down of fat and glycogen in to useful fuel for cells.
  3. Acceleration of heart rate and cardiac output
  4. Increase in blood flow to brain, heart, and skeletal muscles.
  5. The catecholamine surge causes dilation of pupils of new born even in presence of strong light. This helps the infant to develop early bond with the mother.

Thus fetus plays active role in the process of birth (parturition)

Lactation (L. Lactare, to suckle)

Lactation includes both milk secretion by the mammary glands and milk release from the breast.

Mammary glands are compound glands which have got evolved from sebaceous glands (sweat glands). They are specialized to secrete milk.

The mammary glands are present in both sexes but are functional only in females. However by hormonal treatment they can be made functional in males also. (Gynecomastia)

The position of the mammary glands is ventral lateral. In Elephants and primates they are located in the thorasic region. In Ungalates they are located in the inguinal region.

The number of mammary glands is two in man, cow and others giving birth to one or two young ones, whereas in litter bearing animals like dog, cat etc. they are more in number extending from thorasic to inguinal region. In man however supernumerary (more than normal) number of breasts 3, 4, or even six nipples) are not very uncommon.

Between birth to maturity the mammary glands increase in complexity. They develop extensive branched duct system connected to Alveoli like milk secreting gland. There is ample adipose tissue (fat) associated and also connective tissue. In some animals like cows buffaloes etc. the tits are elongated which accumulate more amount of milk.

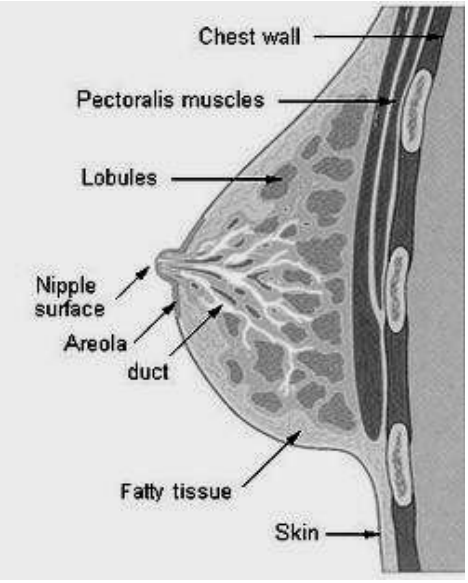


Fig 1.-Human breast

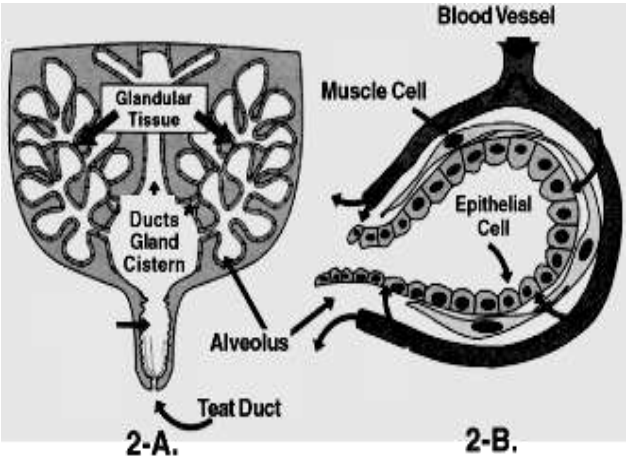


Fig. 2.- Bovine mammary gland

Endocrine control of lactation :

Development of mammary glands – Estrogen and progesterone play important role in the development of mammary glands. However secretions of thyroid and adrenal play important role in making optimal functioning of mammary glands. It has been established that estrogen alone leads to duct growth, however if given larger doses for longer period it can also cause growth of alveolar system. Progesteron alone causes growth of alveolar system. Effect of both the hormones together has synergic effects.

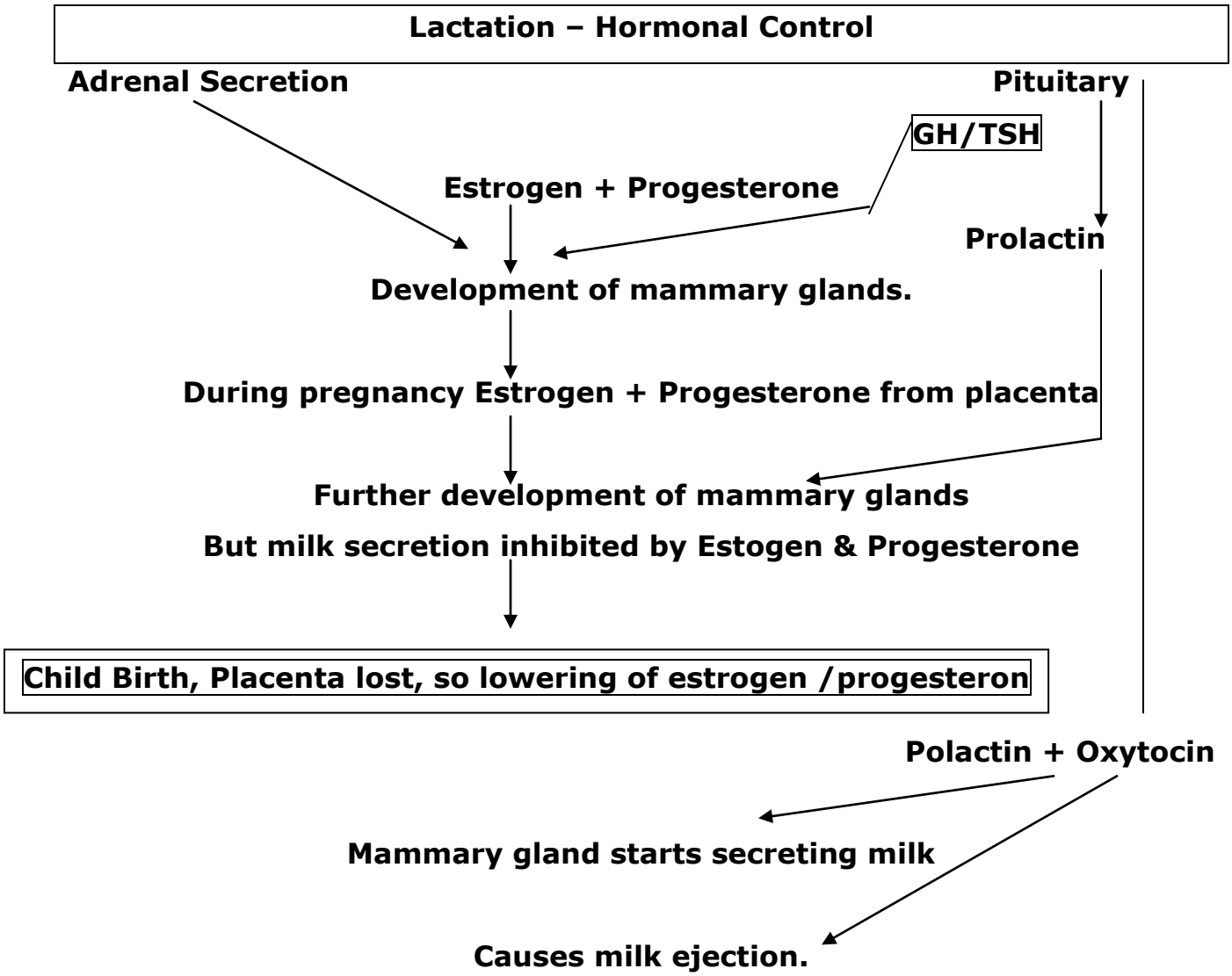
During pregnancy increase in the levels of prolactin cause enlargement of breasts. Apart from this it has been observes in cattle that injection of crude pituitary extract increases the size of mammary glands and also milk production. The main hormones responsible for this are GH (Growth Hormone) and TSH (Thyroid Stimulating Hormone)

During pregnancy though the mammary glands (Breast) develop significantly, milk secretion does not occur because placental secretion of estrogen and progesterone inhibit milk secretion from breast. After child birth, the placenta gets expelled thus dropping the concentration of Estrogen and progesterone which starts secretion of milk.

In women (mother) the breasts do not actually release milk until 1 to 3 days after the baby is born. During these first days, the suckling baby receives

colostrums, a high protein fluid present in the breast at birth. It contains abundant maternal antibodies and thus helps strengthen the baby's immune system. It also functions as laxative, removing fetal wastes, called meconium, retained in the intestine.

After about 3 days, the prolactin secreted from pituitary stimulates milk production. The newborn's suckling stimulates the pituitary to release oxytocin as well as prolactin. Oxytocin triggers milk release from the mammary glands.


Lactation – Hormonal Control
Adrenal Secretion
Pituitary
GH/TSH
Estrogen + Progesterone
Prolactin
Development of mammary glands.
During pregnancy Estrogen + Progesterone from placenta
Further development of mammary glands
But milk secretion inhibited by Estogen & Progesterone
Child Birth, Placenta lost, so lowering of estrogen /progesteron
Polactin + Oxytocin
Mammary gland starts secreting milk
Causes milk ejection.