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UNIT V (Part I)

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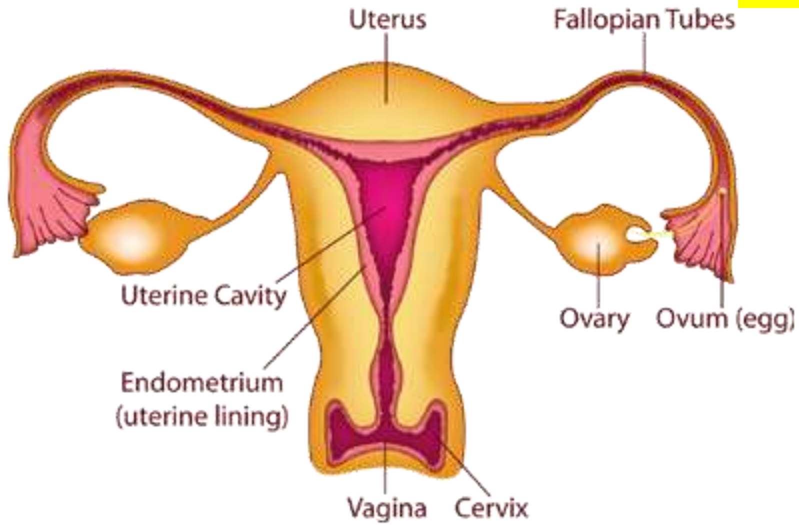
Ovary



Ovaries are part of the vertebrae female reproductive system. Normally, a female will have two ovaries, each performing two major functions: producing eggs, or (exocrine function) and secreting hormones, or (endocrine system). Ovaries in females are homologous to testes in males. The term gonads refer to the ovaries in females and testes in males.

Fimbria is a fringe of tissue near the ovary leading to the Fallopian tubes. When ovulation is about to occur, the sex hormones activate the fimbria, causing it to hit the ovary in a gentle, sweeping motion.

Fallopian tubes, also known as oviducts, uterine tubes, and salpinges, are two very fine tubes leading from the ovaries of female mammals into the uterus.

Uterus: The main function of the uterus is to accept a fertilized ovum, which becomes implanted into the endometrium, and derives nourishment from blood vessels which develop exclusively for this purpose. The fertilized ovum becomes an embryo, develops into a fetus and gestates until childbirth. Due to anatomical barriers such as the pelvis, the uterus is pushed partially into the abdomen due to its expansion during pregnancy. Even in pregnancy the mass of a human uterus amounts to only about a kilogram. The main function of the uterus is to accept a fertilized ovum which becomes implanted into the endometrium, and derives nourishment from blood vessels

Clitoris: is a female sexual organ. In humans, the visible knob-like portion is located near the anterior junction of the labia minora, above the opening of the vagina. The clitoris does not contain the distal portion of the urethra and functions solely to induce sexual pleasure. The only known exception to this is in the spotted hyena, where the urogential system is modified so that the female urinates, mates and gives birth via an enlarged, erectile clitoris. The clitoris is the main organ of sexual arousal and orgasm in most women.

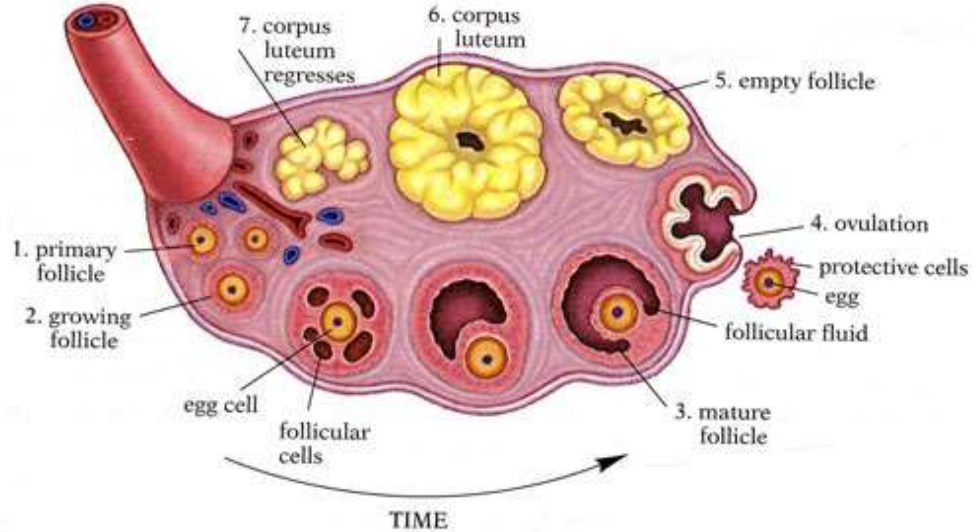
Vulva: is the external genital organs of the female. In human beings this consists of the *labia majora* and *labia minora* clitoris, opening of the urethra, and the opening of the vagina. It protects women's sexual organs and the urinary opening from trauma and infection.

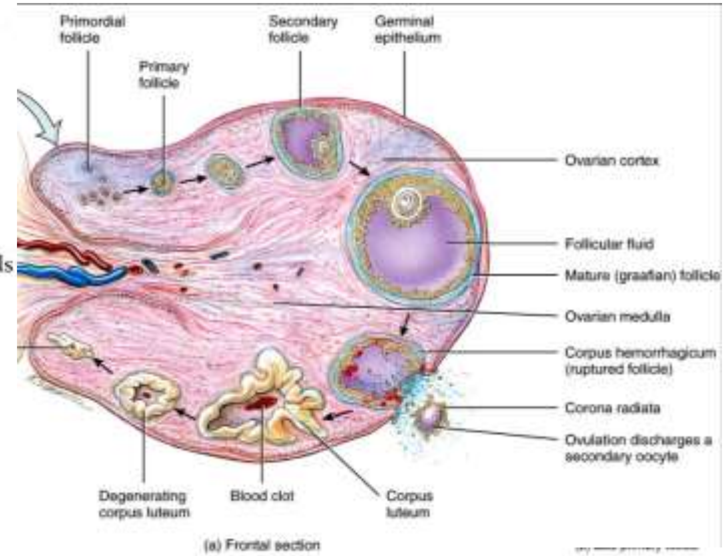
Urethra: is about 1-1.5 inches (2.5-4 cm) long and opens in the vulva between the clitoris and the vaginal opening.

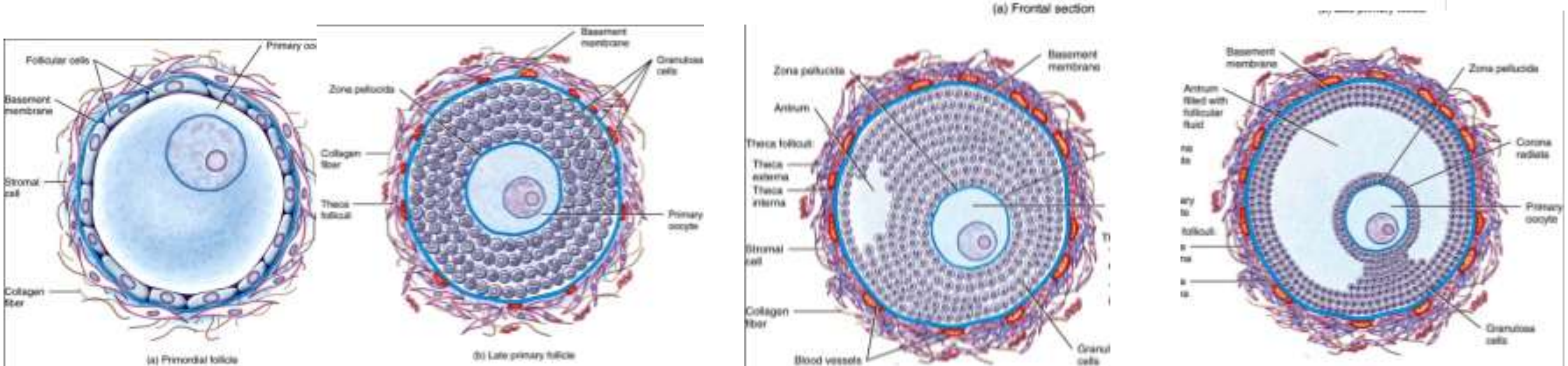
Vagina: During live birth, the vagina provides the route to deliver the fetus from the uterus to its independent life outside the body of the mother. During birth, the vagina is often referred to as the birth canal.

Cervix: The opening from the vagina into the womb allows menstrual blood exit and sperm in.

Anatomy of ovary







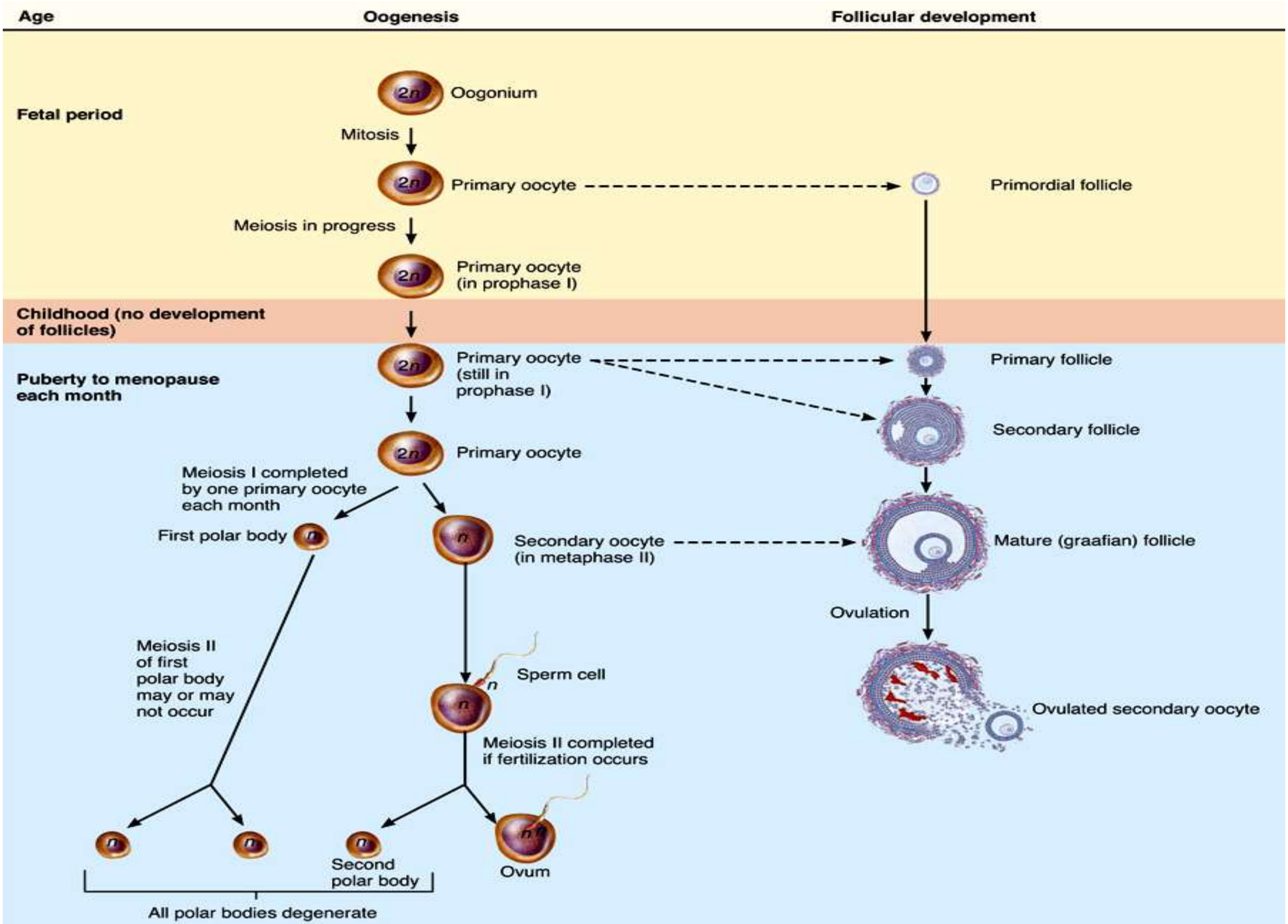
- Each ovary is about the size and shape of an almond. In young women the ovaries are about 1½ - 2 inches long, 1 inch wide & 1/3 inch thick. After menopause they tend to shrink. Covered by Germinal epithelium
- Ovarian cortex: Ovarian follicles of various stage (primordial, primary, secondary preantral, secondary antral, tertiary and graafian), corpus luteum and stromal cells
- Ovarian medulla: Contains blood vessels, lymphatic vessels, and nerves
- They produce eggs (also called ova). Every female is born with a lifetime supply of eggs
- Ovary also produce hormones: Estrogens, Progesterone, inhibin and relaxin
- Gametogenic potential of the ovary is established early in fetal development, but the endocrine role of the ovary is not realized until puberty.

Oocyte and follicular development

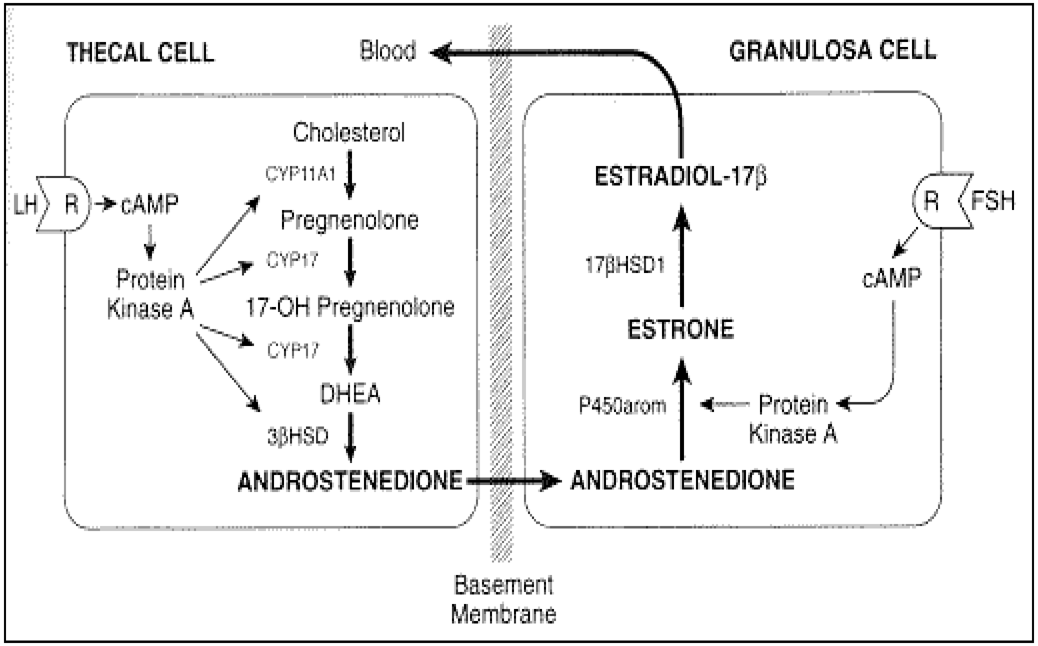
- They are among the first organs to be formed as the female baby develops in the uterus. At 20-week, the structures that will become the ovaries having millions of potential egg cells. The number begins to decrease rapidly. A newborn infant has about 1 million to 2 million egg cells. By puberty the number remain only to 300,000. For every egg that matures and undergoes ovulation, roughly a thousand will fail, so that by menopause, only a few thousand remain.
- A total of only 400 to 500 oocytes are released from the ovaries, the remaining 99.9% undergo atresia during the years of ovarian cycle
- The ovaries produce hormones throughout the fertile period of a woman's life. It is the hormones that control the menstrual cycle. As women get older and menopause approaches, the ovaries make less and less of these hormones and the periods eventually stop altogether.
- The ovaries are the main source of female hormones (estrogen and progesterone). These hormones control the development of female body characteristics, such as the breasts, body shape, and body hair. They also regulate the menstrual cycle and pregnancy.
- Ovary consist of bothe epithelial and mesechymal (interstitial tissue or stroma) tissue
- At birth, each oocyte is sorrounded by a single layer of flattened epithelial-derived granulosa cells – called primordial follicle
- Primordial follicle remain in an arrested, which last until puberty or menopouse
- In the embryonic ovary, primordial follicle begin the reduction division of meiosis but it remain arrested in late prophase state
- The follicle and their primary oocytes may continue to increase in size, oocyte become sorrounded by a single layer of cuboidal cells – now called primary follicle
- After puberty, on endocrine stimulation, in 6-12 primary follicles, number of granulosa cells arround the oocyte – now called secondary follicles. During this, oocyte of these follicle complete the first meiotic division forming secondary oocyte and the first polar body
- The granulosa cell of secondary follicle secrete a mucous material around the oocyte called zona pellucida.
- Secondary oocyte enter into second reduction division of meiosis and remain arrested in metaphase (until fertilization) and ovulation occurs
- GC develop a protoplasmic process that penetrate the zona pellucida and make contact with the plasmalemma of the oocyte for nourishment
- If fertilization occurs, second reduction division is completed giving second polar body
- Out of the developing follicle, only one develops into mature follicle others become atretic and disappear
- After rapture of follicle and liberation of ovum, granulosa and theca cells begin to accumulate large quantity of cholesterol from blood (a process called luteinization) leads to the formation of corpus luteum

About 1-2 million at birth, 300,000 remain at puberty, and around 400-500 will mature and released during a lifetime

Summary of the oocyte and follicular development



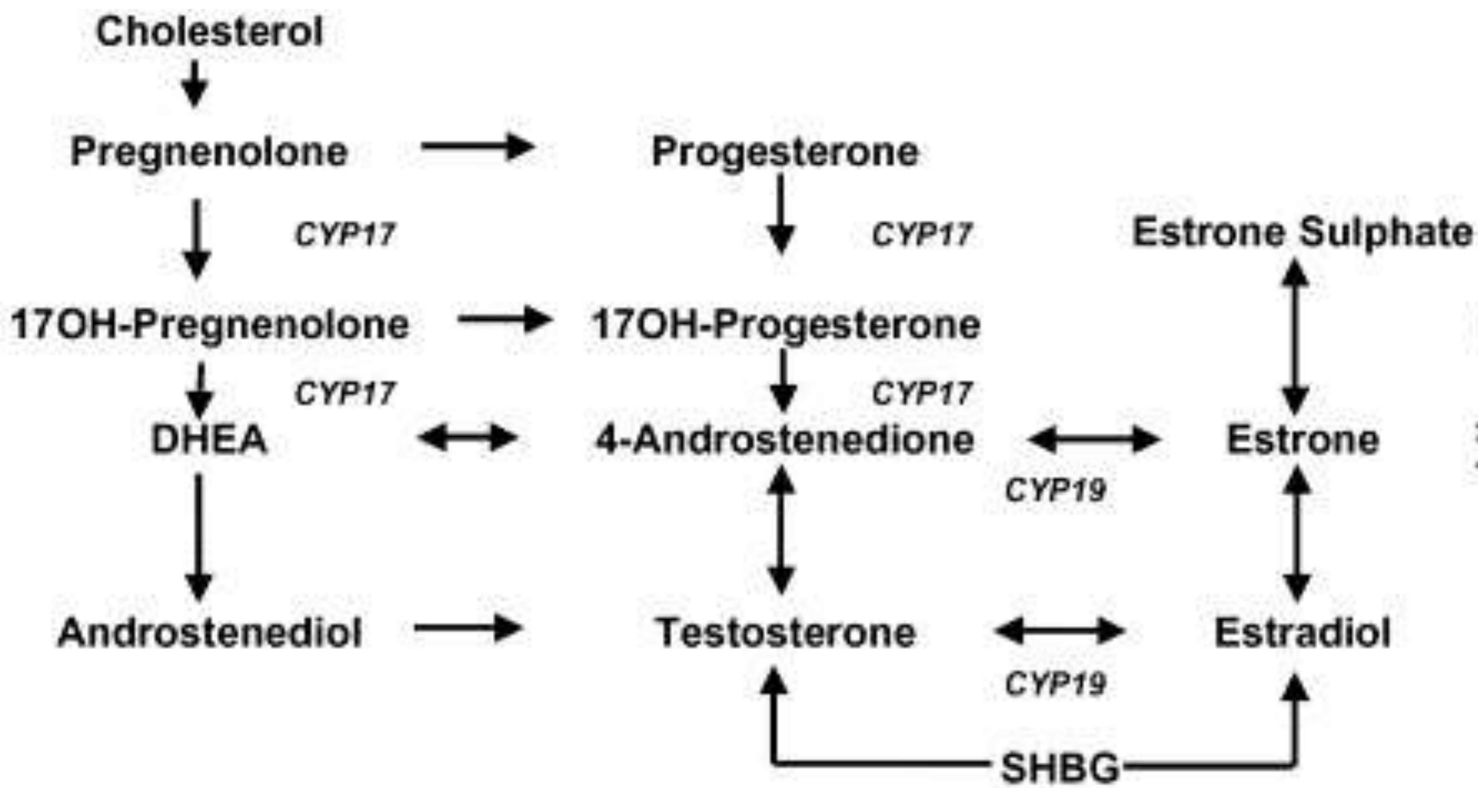
Ovarian Steroid Hormone

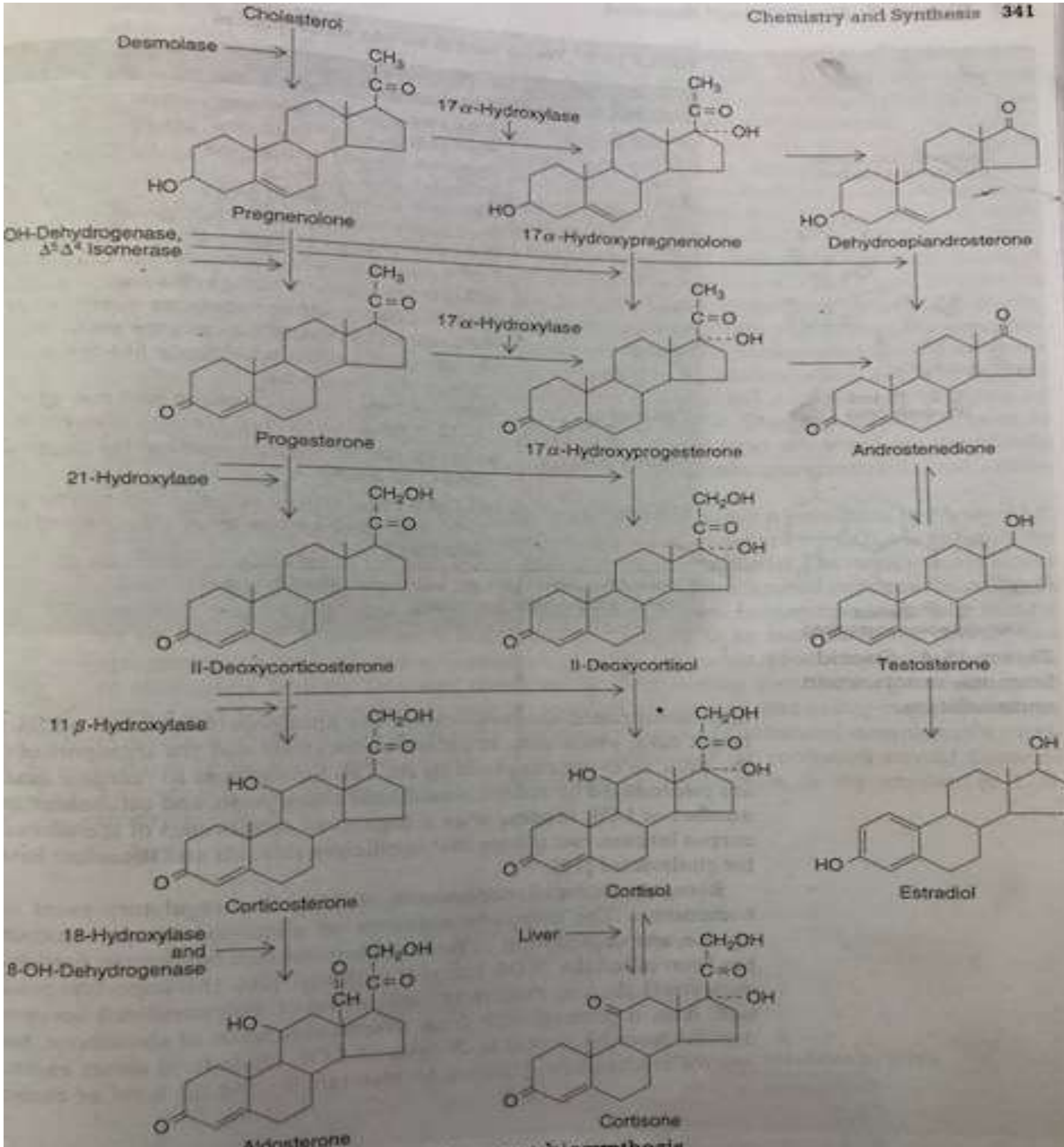


- During the follicular phase, serum estradiol levels and number of granulosa cells increases in parallel.
- FSH receptors exist exclusively on the granulosa cell membranes. Increasing FSH levels during the late luteal phase leads to an increase in the number of FSH receptors and ultimately to an increase in estradiol secretion by granulosa cells
- Increase in FSH receptor numbers is due to an increase in the population of granulosa cells
- During the early follicular phase, LH secretion occurs at a pulse frequency of 60 to 90 minutes with relatively constant pulse amplitude.
- During the late follicular phase prior to ovulation, the pulse frequency of LH increases and the amplitude may begin to increase
- In the presence of estradiol, FSH stimulates the formation of LH receptors on granulosa cells allowing for the secretion of small quantities of progesterone and 17-hydroxyprogesterone (17-OHP) which may exert a positive feedback on the estrogen- primed pituitary to augment luteinizing hormone (LH) release
- FSH also stimulates several steroidogenic enzymes including aromatase, and 3β-hydroxysteroid dehydrogenase (3β-HSD)
- LH receptors are located on theca cells during all stages of the menstrual cycle. LH principally stimulates androstenedione production, and to a lesser degree testosterone production in theca cells.
- Androstenedione is then transported to the granulosa cells where it is aromatized to estrone and finally converted to estradiol by 17-β-hydroxysteroid dehydrogenase type I

- **Principles of Two Cell Theory**
    - **Theca cells get stimulated by LH** – cholesterol from peripheral circulation → androgen
    - **Granulosa cells get stimulated by FSH** – androgen from theca cells → estrogen
    - estrogenic environment **(1)** further enhances aromatase activity (androgen → estrogen) and **(2)** promotes further follicular growth. Androgenic environment has opposite effects (promotes atresia).
    - selection of dominant follicle depends on ability of follicle to establish and maintain estrogenic microenvironment

Biosynthesis and metabolism of estradiol





re 15.3 **Pathways of adrenal steroid hormone biosynthesis.**

Ovarian Steroid Hormone

Ovarian follicles are the source of three types of steroid hormones: progesterone, androgen and estrogens. During follicular phase estradiol is the major steroid hormone while during luteal phase and during pregnancy progesteron is the major hormone secreted

What is estrogen?

Estrogen is a group of female sex hormones that stimulate the appearance of secondary female sex characteristics in girls atpuberty. Estrogen controls controls the growth of the lining of the uterus during the first part of the menstrual cycle, cause breast development in pregnancy and regulates various metabolic processes

Physiological Role of ovarian steroid hormone

During the follicular phase of the menstrual cycle, estrogens are the main steroidal product of the ovary while during luteal phase, progesterone is the main steroid produced by the ovary

Estrogens:

During pubertal maturation: Responsible for growth and development of vagina, uterus and oviduct, and organ essential for ovum transport, zygote maturation and implantation

E effects the distribution of fat deposition in post adolescent female

Mammary gland: In mammary gland cause ductule and stromal growth and development, fat deposition

CNS: Maintain libido (desire) and sexual behaviour, facilitates maternal behaviour, feedback effect

Pituitary: positive and negative feedback effect on gonadotropin secretion, increase pituitary GnRH R number

Increase oxytocin and prolactin production

Ovary: require for ovum maturation

Vagina: causes proliferation and cornification of the mucosa

Oviduct: Causes growth and development of oviduct in preparation for gamete transport

Uterus

Cervix: increase mucous secretion

Endometrium: increse mucous secretion , increase prostaglandin biosynthesis and oxytocin number at term

Myometrium: synthesize contractile protein of smooth muscle cells, increase sensitivity to oxytocin

Skin: sebaceous gland secretion, stimulate axillary and pubic hair growth

Blood: decrease plasma cholesterol formation.

Helps for deveolpment of secondary sexual development

Cause bone mineral deposition, weight gain, female type fat distribution, Maintain bone mineral deposition

Progesterone:

CNS: Increase sexual receptivity in estrogen primed animal, , inhibit balas and gonadotropin secretion during ovarian and luteal phase.

Block release of preovulatory GnRH and gonadotropin surge during pregnancy

Oviduct: cause growth and development of gamete transport

Uterus: It is the ovarian hormone of pregnancy and is responsible for preparing the reproductive tract for zygote implantation and the subsequent maintenance of the pregnant state

Endomertium: stimulate growth and development in preparation for blastocyst implantation.

Cervix: Increase mucous consistancy

Myometrium: decrease sensitivity to oxytocin, decrease estrogen receptor number, maintain pregnancy

Mammary gland: lobular and alveolar development

It trigger sexual behavior in some species

In rodents, it is necessary for induction of sexual receptivity

Play important role in nest-building activity and brooding behavior in some avian species

Causes thermogenic action- rise in metabolic rate

Mechanisms of actions of Estrogen

- Similar to the actions of other steroid hormones, estrogen regulates the transcription of target genes by activating its receptors in the nuclei of target cells
- Two different gene encode the ERα and ERβ
- Unbound receptor is associated with several heat shock proteins (HSPs).
- After entering the cell by passive diffusion through the plasma membrane, the hormone binds to an ER in the nucleus. Binding of estrogen to ER cause dissociation of the receptor from heat shock proteins
- This cause activation of receptor. Hormones receptor complex now binds to specific sequences of nucleotides (estrogen response element)
- The activated receptors then dimerize on the estrogen responsive element on DNA (promoter region of target gene). Dimerization increases the affinity and the rate of receptor binding to DNA
- There is recruitment of co-activators, and some co-regulators to facilitate increased transcription
- The complex together functions as transcriptional machinery
- These altogether activate RNA polymerase and initiates gene transcription
- In ovary, both ERs are expressed but ERα is expressed in thecal and interstitial cells while ERβ is expressed in granulosa cells

Neuroendocrine control of ovarian function

- Activation and maintenance of normal follicular function is dependent on gonadotropins LH and FSH leading to ovulation
- Pituitary gonadotropin secretion is critically dependent on hypothalamic GnRH release
- There is pulsatile pattern of gonadotropin and GnRH secretion
- The neuronal mechanisms that are responsible for generating the pulsatile rhythm of GnRH release is collectively referred to as GnRH pulse generator
- Stress or under nutrition can inhibit the activity of reproductive activity through the retardation of GnRH pulse generator

Menstrual Cyclicity is maintained by ovarian feedback mechanism

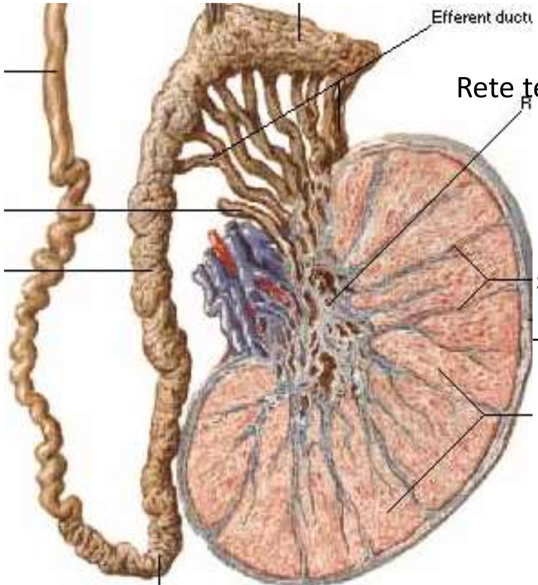
Negative feedback:

- Both progesterone and estrogen exert a negative feedback suppression of gonadotropin secretions during the menstrual cycle
- These feedback maintain a low and slow basal pulsatile LH secretion pattern throughout the follicular and luteal phases of the cycle
- This feedback shows that removal of ovaries results in dramatic rise in LH secretion and replacement with estrogen and progesterone can return LH to basal levels
- Negative feedback exerts at the hypothalamic and pituitary level to suppress both GnRH pulse generator gonadotropin actions respectively
- Progesterone also exerts negative feedback control over pulsatile LH secretion particularly during luteal phase of the cycle

Positive feedback:

- The maturing follicle secretes high level of estrogens the stimulates the abrupt release of mid-cycle preovulatory LH surge
- This stimulatory action of estrogen is referred to as positive feedback
- Estrogen clearly acts on the pituitary gland where it stimulates LH secretion, that has stimulatory action on GnRH
- Some of the positive feedback effect at the hypothalamic level and evoke GnRH surge which in turn stimulate LH surge
- Low level of estrogen during the early follicular phase of the menstrual cycle exert negative feedback action that maintains a basal level of gonadotropin secretion
- But by the late follicular phase, the maturing follicle produces increased amount of estrogen
- After 36 hour estrgen level becomes critical and the negative feedback is reversed and positive feedback is ensued
- This results in release of preovulatory gonadotropin surge. This cause ovulation, source of estrogen is not no more
- CL is formed and progesterone reestablishes negative feedback
- The sum of both processes is approximately 28 days

Testis



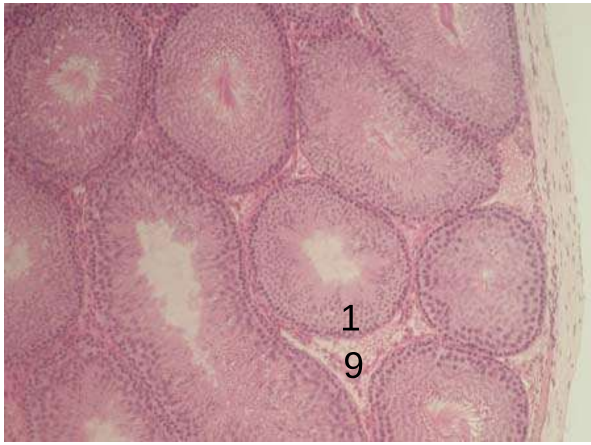
- The **testis** is covered by a dense collagenous coat called the **tunica albuginea**. Septa extend into the testis to separate the lobules. In mature testis, there is a prominent vascular layer immediately beneath the tunica albuginea. It consists of semniferous. SEMINIFEROUS TUBULES – PRODUCES SPERMS OR SPERMATOZOA.

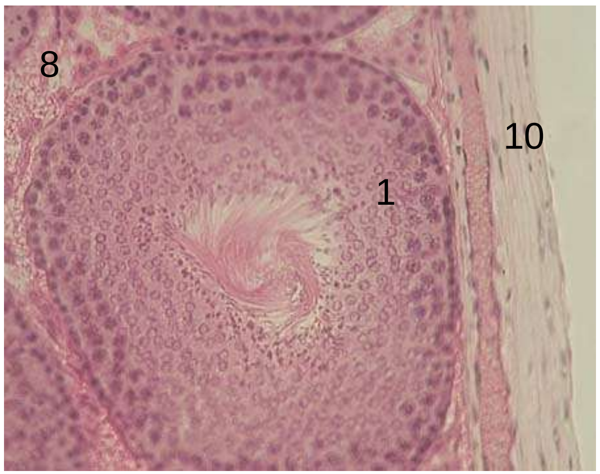
- Most of the testis is occupied by highly coiled **seminiferous tubules.** IT PRODUCES SPERMS OR SPERMATOZOA. EPIDIDYMIS – A TEMPORARY STORAGE PLACE OF SPERMS

- The abundant seminiferous tubules all lead into the mediastinum of the testis, separated from the rest of the testis by the tunica albuginea as well. The mediastinum includes the rete testis, which lead to the efferent ducts and then the epididymis at the posterior aspect of the testis. The epididymis can be divided into three parts – the head, the body, and the tail. IT – NARROW TUBE, FOUND ON TOP OF THE TESTES; WHERE SPERM CELLS ARE COLLECTED; WHERE CELLS MATURE FINALLY AND BECOME READY FOR TRANSPORT

- The ductus deferens is continuous with the tail of the **epididymis**. ITS AN ORGANS FOR SPERM TRANSPORT. It joins the duct of the seminal vesicle to form the ejactulatory duct.

Ultra structure of testis





- The **seminiferous tubules** are composed of **spermatogonia** located at the base of the epithelium with large round nuclei.

- Spermatogonia give rise to **primary spermatocytes**, with larger nuclei midsway up in the epithelium. The nuclei are round with distinct bundles of dense chromosomes. These cells are in extended prophase of the first meiotic division. The primary spermatocytes further develop into secondary spermatocytes

- The secondary spermatocytes further develop into **spermatids** located higher up in the epithelium toward the lumen. The round nuclei of sparmatid become smaller, denser, and change shape into the heads of mature **sperm**, or spermatozoa.

- Also found within the seminiferous tubules are **Sertoli cells**, which are large, relatively pale and irregularly shaped. We can see a prominent nucleolus within the Sertoli cell nucleus. These cells primarily support and nourish the germ cells in the testis with long, apical cytoplasmic folds. They contain testosterone and FSH receptors

- Within the loose connective tissue of the testis, among seminiferous tubules, we can see **Leydig cells**. These cells secrete the male steroid hormone, testosterone. There may be small capillaries found among the clusters of Leydig cells.

-Blood capillaries are not found inside the semniferous tubules, hence there is blood testis barrier.

1- seminiferous tubule
2 - spermatogonia
3 - primary spermatocytes
4 - secondary spermatocytes
5 - spermatids
6 - spermatozoa
7 - Sertoli cells
8 - Leydig cells
9 - Interstitium
10 - Tunica albuginea

Source and Synthesis of androgens

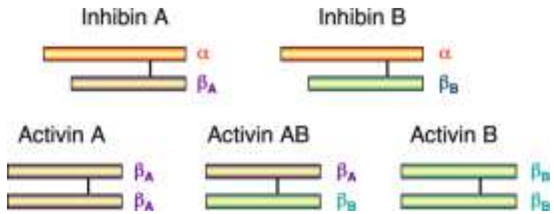
- Testosterone is the main male steroid hormone produced by the testis
- Cholesterol serves as the substrate for pregnenolone biosynthesis in the Leydig cells
- Cholesterol is converted to pregnenolone or to progesterone, which is further converted to 17-hydroxylated steroids
- 17-hydroxylated steroids is converted to Dehydroepiandrosterone (DHEA), which converted to androstenedione and then to testosterone
- Androstenedione and DHEA are also released into blood but the physiological potencies of these androgens are so low that they will not substitute for normal Leydig cell functions
- Almost 100% testosterone remain bound with protein: 40% with b-globulin called gonadal steroid-binding globulin, 40% with albumin, 17% with other proteins

Activin and **inhibin** are two closely related protein complexus that have almost directly opposite biological effects both dimeric in structure, and, in each complex, the two monomers are linked to one another by a single disulfide bond

Inhibin exerts negative feedback actions on pituitary FSH secretion:

- The Sertoli cells of the testes produce a peptide hormone, Inhibin. Inhibin inhibits FSH secretions in both male and female.
- Thus a reciprocal relationship between FSH and inhibin exists
- Both produces compensatory changes in the other

- Inhibin is composed of two polypeptides, one a and one b subunit.
- In mammals, four beta subunits have been described, called activin β_A, activin β_B, activin β_C and activin β_E.
- A fifth subunit, activin β_D, has been described in *Xenpus laevis*.
- There are two forms of b subunit, bA and bB are predominant.
- The a subunit combines with bA to form inhibin A and with bB to form inhibin B
- Inhibin B is predominant form
- but not all theoretically possible, heterodimers have been described
-
- Another hormone is also produced called Activin that stimulates FSH secretions
- Activin is formed by dimerization of b subunits of inhibin
- bA- bB combines to forms activin A
- bB- bB combines to form activin B
- bA- bB combines to form activin AB



- **Ovarian Inhibin:** Inhibin is present in follicular fluid, GC extract, oavrian venous plasma.
- Supressive effect on both basal and GnRH stimulated pituitary FSH secretion
- FSH stimulation induce inhibin secretion and inhibin acts to suppress FSH secretion- negative feedback loop
- During ovulatory phase the conc. of inhibin drops down as a consequence of preovulatory LH surge for recuuitment of new follicles

Inhibin is produced in the gonads, pituitary gland, placenta, corpus luteum and other organs.

FSH stimulates the secretion of inhibin from the granulosa cells of the ovarian follicles in the ovaries. In turn, inhibin suppresses FSH.

Inhibin B reaches a peak in the early- to mid-follicular phase, and a second peak at ovulation.

Inhibin A reaches its peak in the mid-luteal phase.

Inhibin secretion is diminished by GnRH, and enhanced by insulin-like growth factor (IGF-1).

Testicular Inhibin: It is secreted from the Sertoli cells, located in the semniferous tubules inside the testes. Androgen stimulate inhibin production; this protein may also help to locally regulate spermatogenesis.

Clinical significance

Inhibin

Quantification of inhibin A is part of the prenatal quad screen that can be administered during pregnancy at a gestational age of 16–18 weeks.

An elevated inhibin A (along with an increased beta-HCG, decreased AFP, and a decreased estriol is suggestive of the presence of a fetus with Down syndrome.

It also has been used as a marker for ovarian cancer

Inhibin B may be used as a marker of sspermatogenesis function and male infertility.

inhibin B level is significantly higher among fertile men (approximately 140 pg/mL)

infertile men (approximately 80 pg/mL)

Activin Stimulates FSH biosynthesis

•In the ovarian follicle, activin increases FSH binding and FSH-induced aromatization. It participates in androgen synthesis enhancing LH action in the ovary and testis. In the male, activin enhances spermatogenesis.

•Lack of activin during development results in neural developmental defects.

•Upregulation of Activin provides a useful tool for stem cell ddifferentiation and oorganoid formation.

•Activins interact with two types of cell surface transmembrane receptor (Types I and II)

Activin type 1 receptor: ACVR1, ACVR1B, ACVR1C

Activin type 2 receptor : ACVR2A, ACVR22B

Clinical significance

Activin A is more plentiful in the adipose tissue of obese, compared to lean persons.

promotes the proliferation of adipcyte progenitor cells,

inhibiting differentiation into adipocytes.

A mutation in the gene for the activin receptor ACVR1 results in fibrodysplacia_ossificans progressiva. causes muscle and soft tissue to gradually be replaced by bone tissue. formation of an extra skeleton that produces immobilization and eventually death

Endocrine control of testicular function

The testis has two major functions: androgen production and spermatogenesis

Male Reproduction function in maintained by a "Hypothalamic-Pituitary-Testicular Axis" of hormones:

- Pituitary gonadotropins, LH and FSH control both steroidogenic and spermatogenic functions of the testis
- Gonadotropin are in turn controlled by release of GnRH
- GnRH receptors are present on gonadotropes thereby stimulate the synthesis and secretion of gonadotropins, LH and FSH
- LH receptors are present on Leydig cells and FSH receptors are present on Sertoli cells
- LH primarily stimulates steroidogenesis and testosterone secretion from Leydig cells and FSH suppotrts the development of spermatogenic activity of sertoli cell
- Pituitary gonadotropin secretion is enhanced after orchidectomy, where as gonadotropin secretion dimnished after administration of exgenous androgens. This suggests that testicular androgen exert a negative feedback on pituitary gonadotropin secretion

negative feedback actions on pituitary FSH secretion:

- The Sertoli cells of the testes produce a peptide hormone, Inhibin. Inhibin inhibits FSH secretions
- Thus a reciprocal relationship between FSH and inhibin exists
- Both produces compensatory changes in the other
- Inhibin is composed of two polypeptides, one α and one β subunit. There are two forms of β subunit, βA and βB
- The α subunit combines with βA to form inhibin A and with βB to form inhibin B
- Inhibin B is predominant form
- Another hormone is also produced called Activin that stimulates FSH secretions
- Activin is formed by dimerization of β subunits of inhibin
- βA- βB combines to forms activin A
- βB- βB combines to form activin B
- βA- βB combines to form activin AB

Prolactin regulate LH receptor number in Leydig cells:

Inhibition of Prolactin secretion results in decreased number testicular LH receptors
While Prolactin prevents loss of LH receptors
Therefore Prolactin plays a role in the control of testicular LH receptor number in Leydig cells

Physiological Roles of Androgens

Testicular androgens are responsible for the growth and development of those tissues and organs that characterize the male, male urinogenital system, the accessory sex organs and the external genitalia

Spermatogenesis:

During puberty, initiation of spermatogenesis requires FSH. But it can be maintained in hypophysectomized adult animal only by testosterone, in the absence of FSH . FSH interacts with Sertoli cells plasma membrane receptor results in cAMP production and synthesis of androgen binding protein (ABP). ABP is then secreted into the lumen of semniferous tubules. LH receptor present on Leydig cells. In response to LH, Leydig cells produces testosterone. Testosterone enters into systemic circulation and to the adjascent semniferous tubules. Testosterone is taken up by Sertoli cell by active transport mechanism or by facilitated diffusion. Within Sertoli cells , testosterone remain bound to ABP. Because germ cells lack androgen receptor, but it is developed into mature spermatozoa in the presence of Sertoli cells. It is presumed that hormonal effect of testosterone on spermatogenesis are mediated via Sertoli cells. ABP functions to transport testosterone to the epididymis where spermatozoa matures.

Testosterone modulate reproductive behavior and sexual function:

Unlike female, gonadal steroids do not exert positive feedback actions in the pituitary or the hypothalamus of the male to stimulate cyclic release of pituitary hormone surge. Pituitary gonadotropin secretion increased after gonadoectomy, and exogenous androgens depress the elevated gonadotropin secretion in castrated male. Therefore testicular androgens exert a negative feedback actions on pituitary gonadotropin secretion.

- In dove, male courtship is dependent on the action of androgens on preoptic area of hypothalamus
- It increases the copulatory behaviour in rat by acting on the motor neurons that innervate the perineal striated muscle of penis
- In *Xenopus laevis*, androgen regulate mating behavior by action on spinal neurons that control muscle activity of amplexus during mating
- Testosterone alters preoptic neuron responses to natural sexual odors (pheromones), cues importan for reproductive success
- Gonadal androgens are essential for establishment and maintenance of male dominance and sexual aggressive behavior in most birds (domestic fowl)
- Androgens in female phalarope are responsible for inducing nuptial plumage and dominant mating behavior during the breeding season

Androgen action in fetal brain program sexual orientation:

Interior nuclei of anterior hypothalamus is responsible for sexual orientation formed very early during development and as twice as large in normal male that than in female. It is under the effect of androgen.

Testosterone stimulate development of male secondary sex characteristics:

Dimorphic secondary sex characteristics are typical of all vertebrates: skin coloration; hair color, distribution and coarseness; development of specilized integumental structures such as horns, antlers, beaks, claws; courtship behavior such as aggression, body movement and display and even vocalization.

Sex organs: Accessory reproductive glands prostrate, seminal vesicles and bulbourethral glands that contribute to the secretory product of semen are dependent on testosterone. Eg, Semial vesicle secretes fructose a source of metabolic energy for developing spermatozoa

Skin: sebaceous gland activity is stimulated by testosterone. Acne present in the male during puberty is due to increased activity of sebaceous gland in response to elevated plasma level of androgens
Coarseness and pattern of hair on body and face are increasedc by androgens
Androgen cause baldness in male with genetic prediposition. Castration prevent the further extension of baldness in these males.. In female due to adrenal virilism the excessive level of androgen induce baldness
Skin, hair and feather coloration differ between the sexes in some teleosts and birds due to pigmentary changes are androgen dependent.

Sexually dimorphic kidney: Proximal cnovulated tubule of kidney of male mice contain mitochondria and lysosomes that are structurally different from those of the females

Submaxillary glands of mice: submaxillary glnds produce nerve growth factor and epidermal growth factor are controlled androgens in mice. Some enzymes are more abundant in male than in females

Brood patches: some birds (where male incubate eggs) develop brood patches on the abdomen during breeding season. Feather are lost from these areas and skin becomes thick and hypervascularized that imparts warmth to the incubating eggs. In birds where both sexes incubate eggs both androgen and estrogen develop patches

Epidermal cornifications: In amphibians, nuptial pads that helps in grasping the female during amplexus are androgen dependent

Antlers: growth and shedding of antlers, outgrowth of integument in male deer develop during the breeding season are controlled by androgens

Androgen exert anabolic actions in muscles, cartilage and other tissues:

Major extragenital sites sites of androgen action is skeletal muscle
Growth of musculature and cartilage of the larynx in human cause permanent deepening of the voice. Testosterone has direct anabiloc action on these muscles.

References:

Endocrinology, Hadley M. E. and Levine J.E. 2007, 6th Edition

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