Human Reproduction Physiology

Dr. A. K.Goudarzi, D.V.M. Ph.D
Department of Basic Sciences
I.A. University

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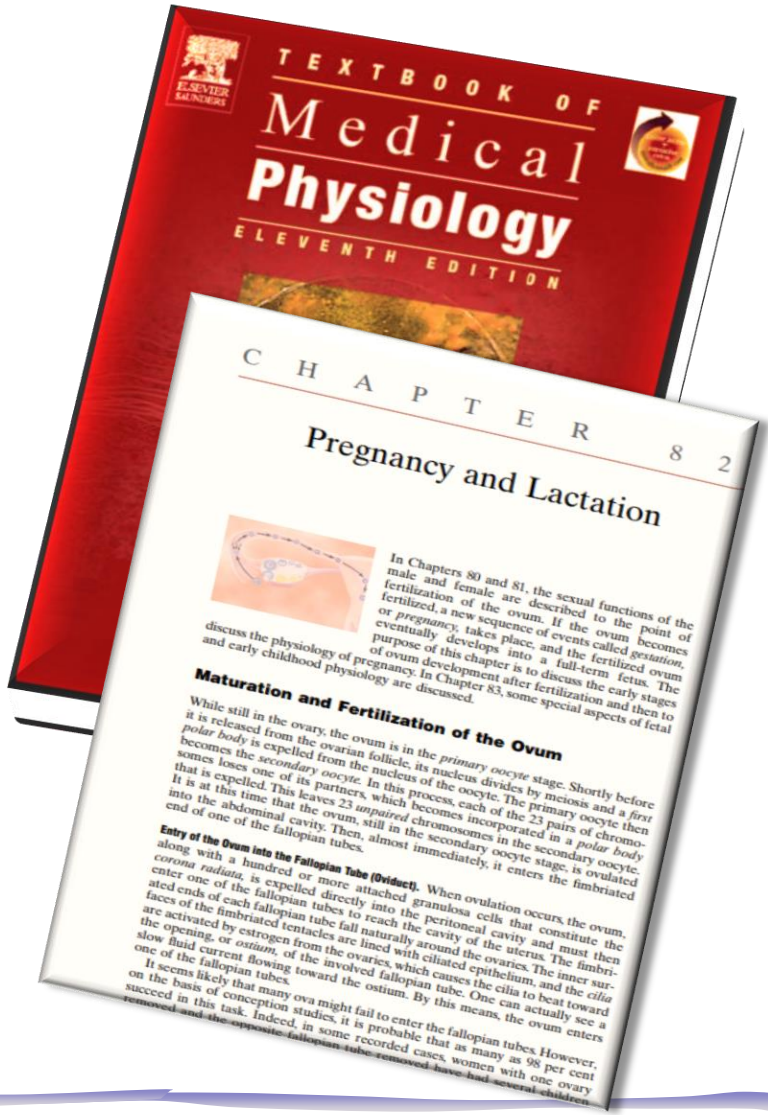
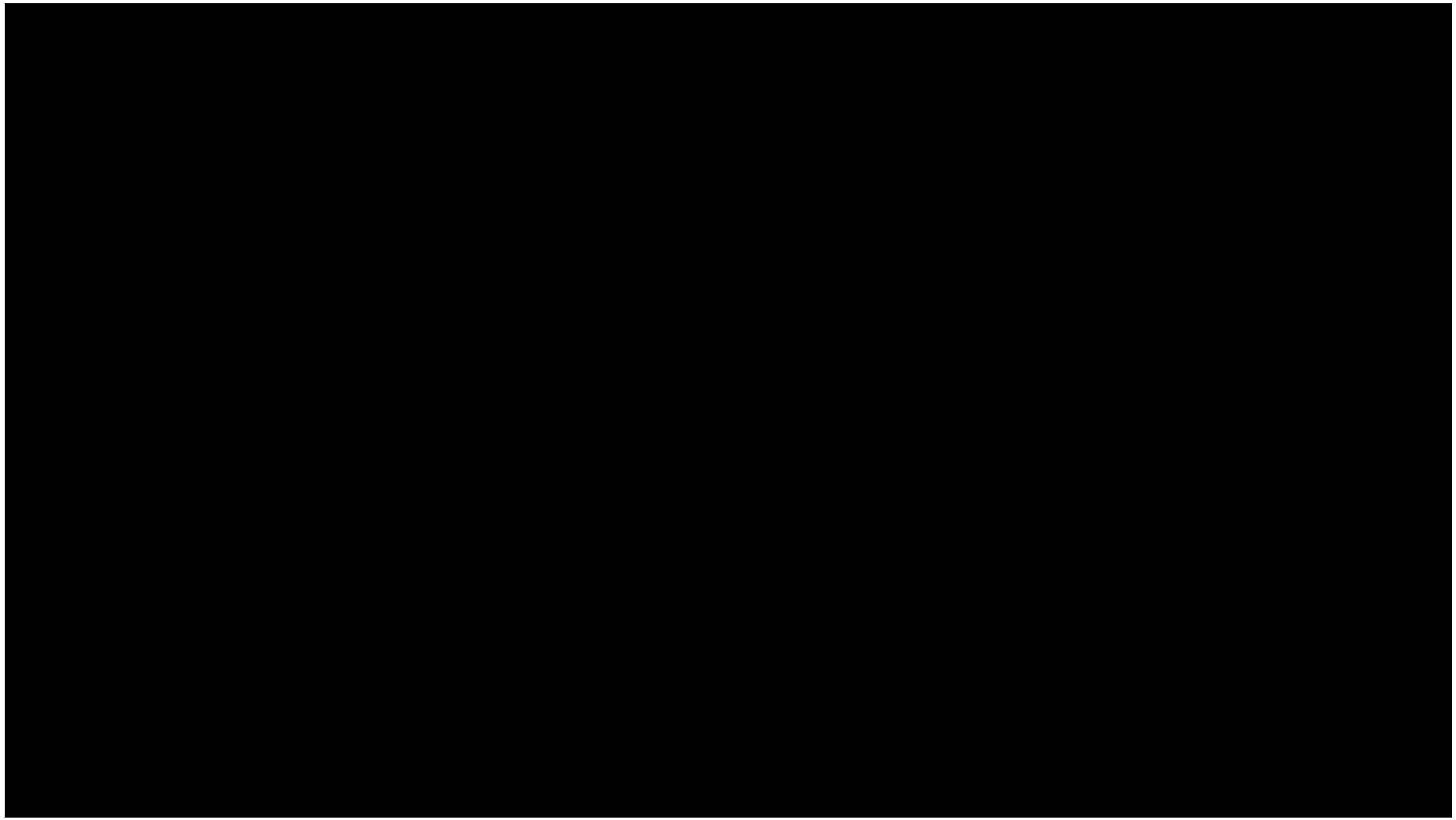


Introduction

Sex Determination and Differentiation

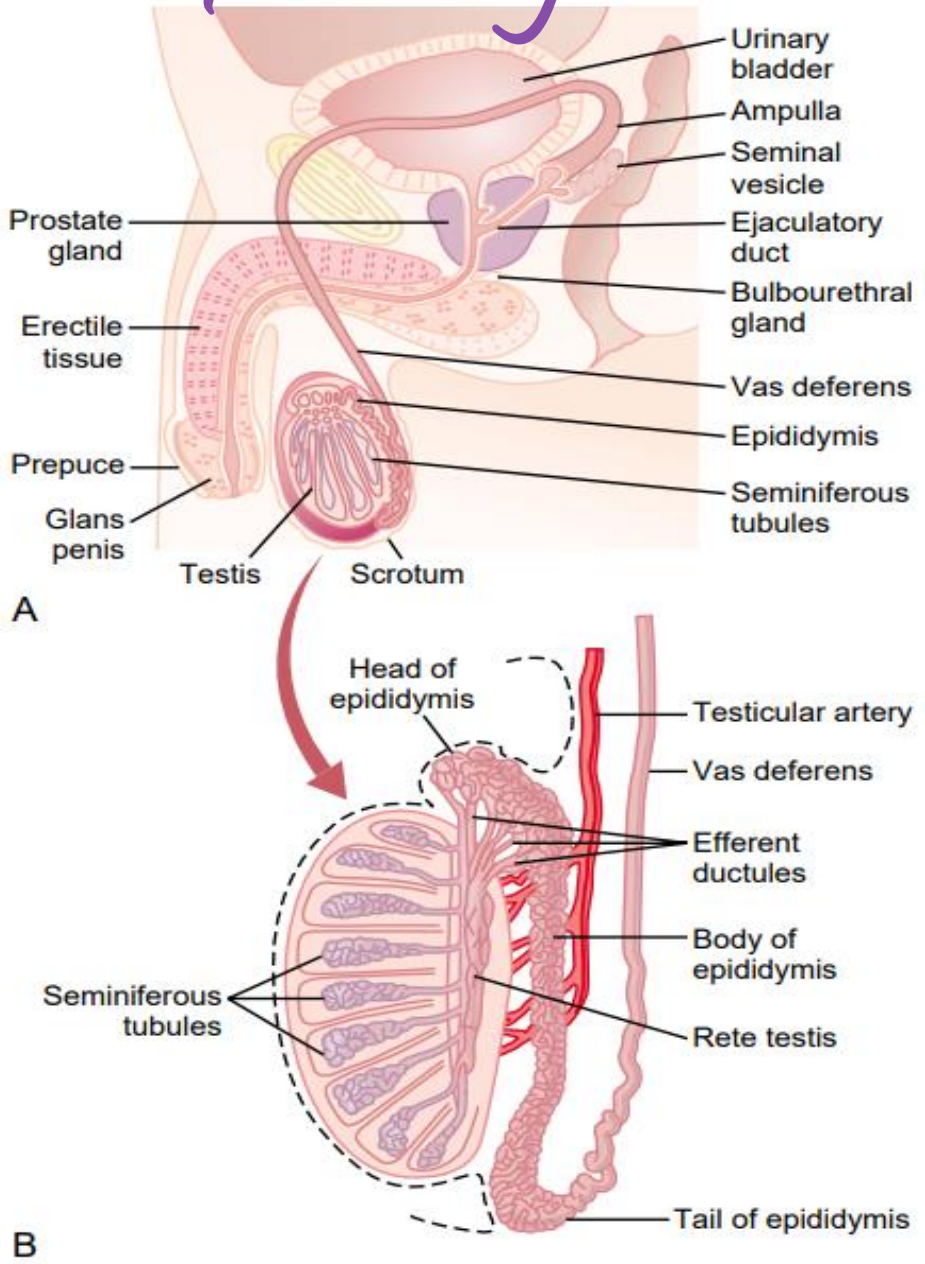


Intersex Phenomenon

Male Reproductive Physiology

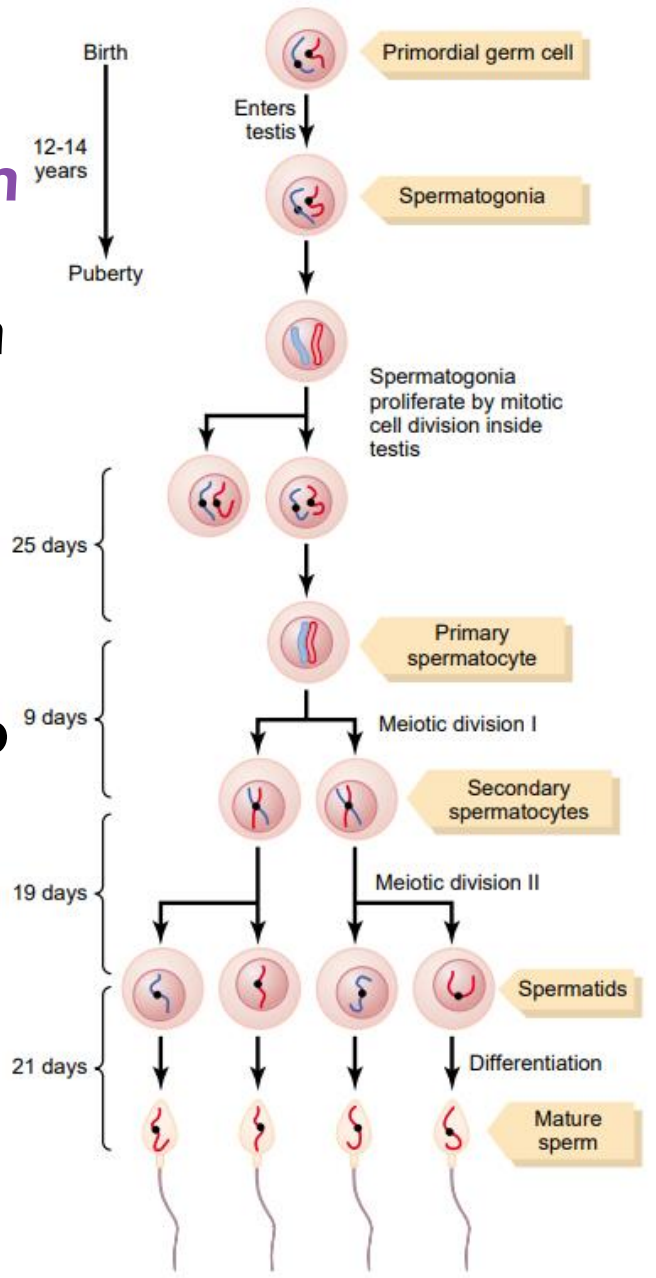
Physiologic Anatomy of the Male Sexual Organs

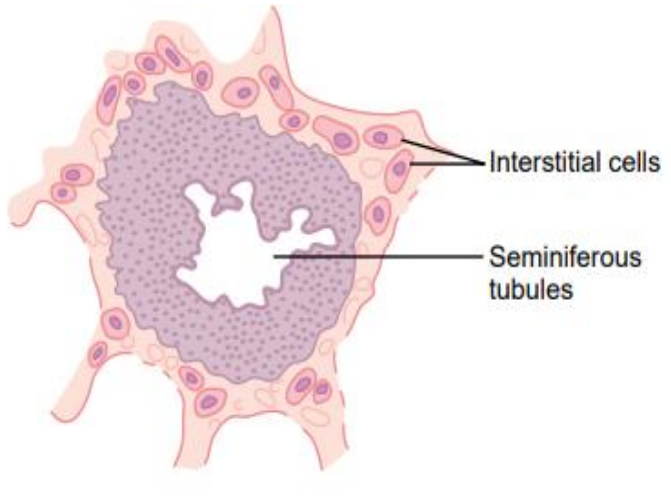
- Testis (Pl.=Testes)
  - Scrotum
  - Seminiferous Tubules
  - Rete Testis
  - Interstitial (Leydig) Cell, Sertoli Cell
- Epididymis
  - Head, Body, Tail
- Vas Deferens
- Ampulla
- Seminal Vesicles
- Prostate gland
- Bulbourethral gland
- Penis
  - Prepuce, Glans Penis, Erectile tissue

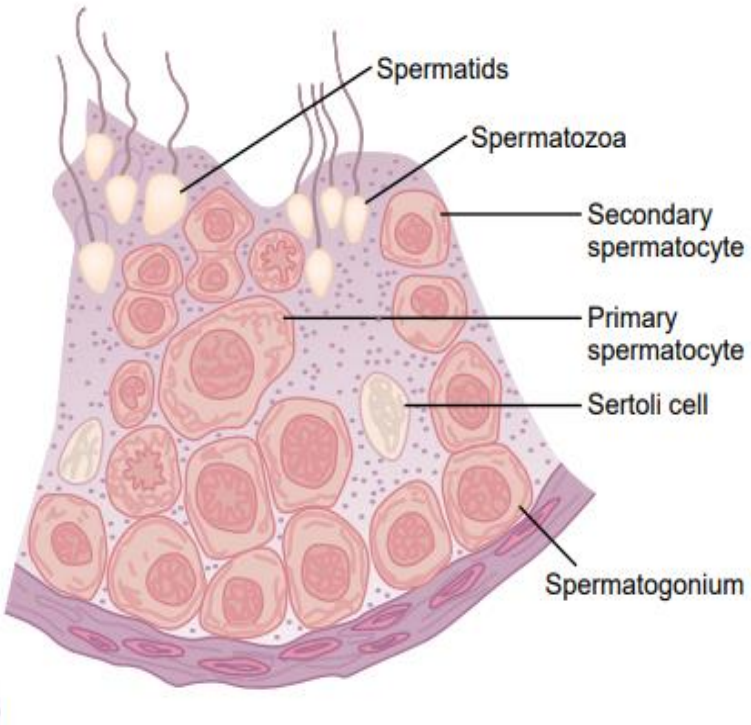


Spermatogenesis

- During formation of the embryo, the primordial germ cells migrate into the testes and become immature germ cells called spermatogonia which lie in two or three layers of the inner surfaces of the seminiferous tubules
- The spermatogonia begin to undergo mitotic division, beginning at puberty, and continually proliferate and differentiate through definite stages of development to form sperm

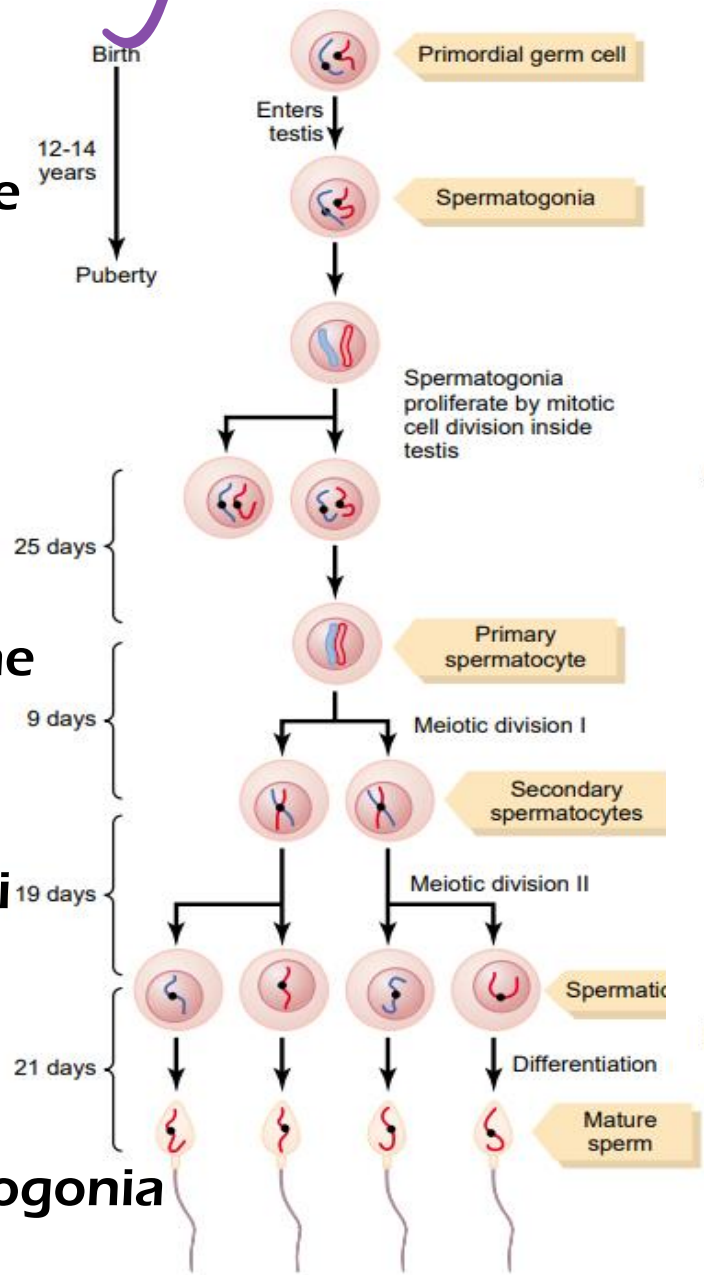


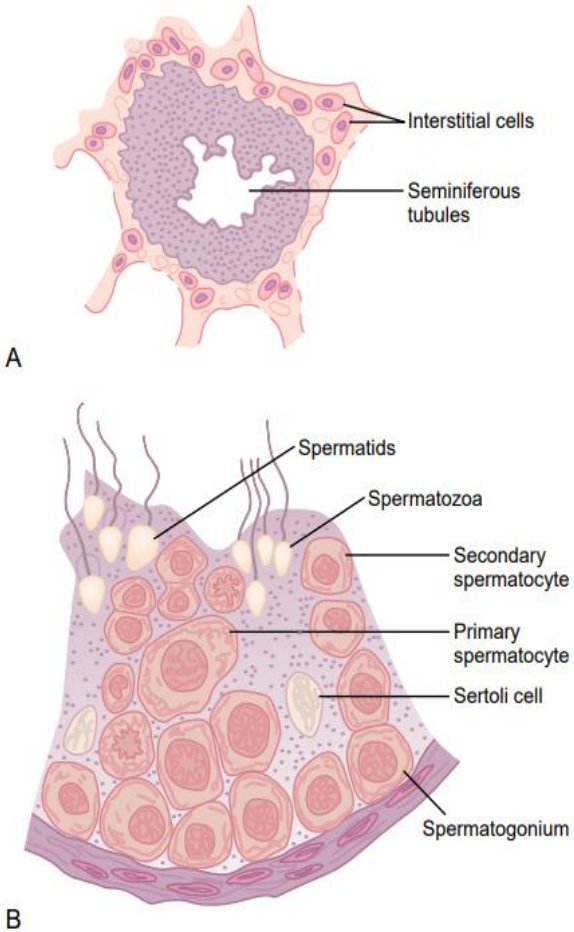




Hormonal effects on Spermatogenesis

- Testosterone
  - essential for growth and division of the testicular germinal cells
- LH (Luteinizing Hormone)
  - stimulates the Leydig cells to secrete testosterone
- FSH (Follicle Stimulating Hormone)
  - stimulates the Sertoli cells to convert the spermatids to sperm
- Estrogens
  - formed from testosterone by the Sertoli cells, stimulated by FSH, and probably essential for spermiogenesis
- GH (Growth Hormone)
  - promotes early division of the spermatogonia





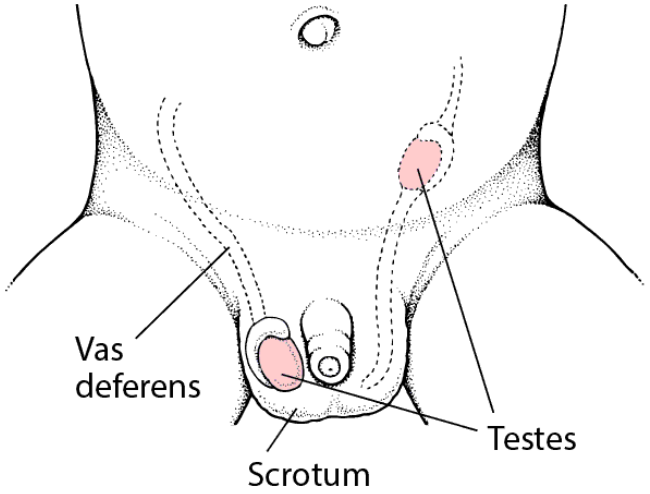
Abnormal Spermatogenesis and Male Fertility

Effect of Temperature on Spermatogenesis

- Increasing the temperature of the testes can prevent spermatogenesis by causing degeneration of most cells of the seminiferous tubules besides the spermatogonia.
- the scrotum acts as a cooling mechanism for the testes.

Cryptorchidism

- At about 3 weeks to 1 month before birth of the baby, the testes normally descend through the inguinal canals into the scrotum.
- Failure of a testis to descend from the abdomen into the scrotum at or near the time of birth of a fetus is called cryptorchidism.
- The remained testis is incapable of forming sperm which leads to sterility.
- operation is done to relocate the cryptorchid testes from the abdominal cavity into the scrotum before the beginning of adult sexual life



Abnormal Spermatogenesis and Male Fertility

Effect of Sperm Count on Fertility

- Semen volume: ≈ 3.5 ml
- Average sperm number in each ejaculation: ≈ 400 million
- Sperm count less than 20 million/ml: infertility

Effect of Sperm Morphology and Motility on Fertility

- Abnormal morphology, such as having two heads, abnormally shaped heads, or abnormal tails can be the cause of infertility
- Sometimes, they are either entirely nonmotile or relatively nonmotile.
- Whenever the majority of the sperm are morphologically abnormal or are nonmotile, the person is likely to be infertile, even though the remainder of the sperm appear to be normal

Male Sexual Act

Neuronal Stimulus for Male Sexual Act

- glans penis:
  - Especially sensitive sensory end-organ system
  - Send sexual signals to the sacral portion of the spinal cord and then to the brain
  - Adjacent areas to the penis (anal epithelium, the scrotum, and perineal structures) can also send stimulating signals to the spinal cord
  - Internal structures, such as in areas of the urethra, bladder, prostate, seminal vesicles, testes, and vas deferens can even originate sexual sensation
  - Some "aphrodisiac" drugs, such as cantharidin, increase sexual desire by irritating the bladder and urethral mucosa, inducing inflammation and vascular congestion
- Psychic Element:
  - Thinking sexual thoughts or even dreaming of the act of intercourse
  - Brain function is probably not necessary for sexual act because appropriate genital stimulation can cause ejaculation in some animals and occasionally in humans after their spinal cords have been cut above the lumbar region

Male Sexual Act

Stages of the Male Sexual Act

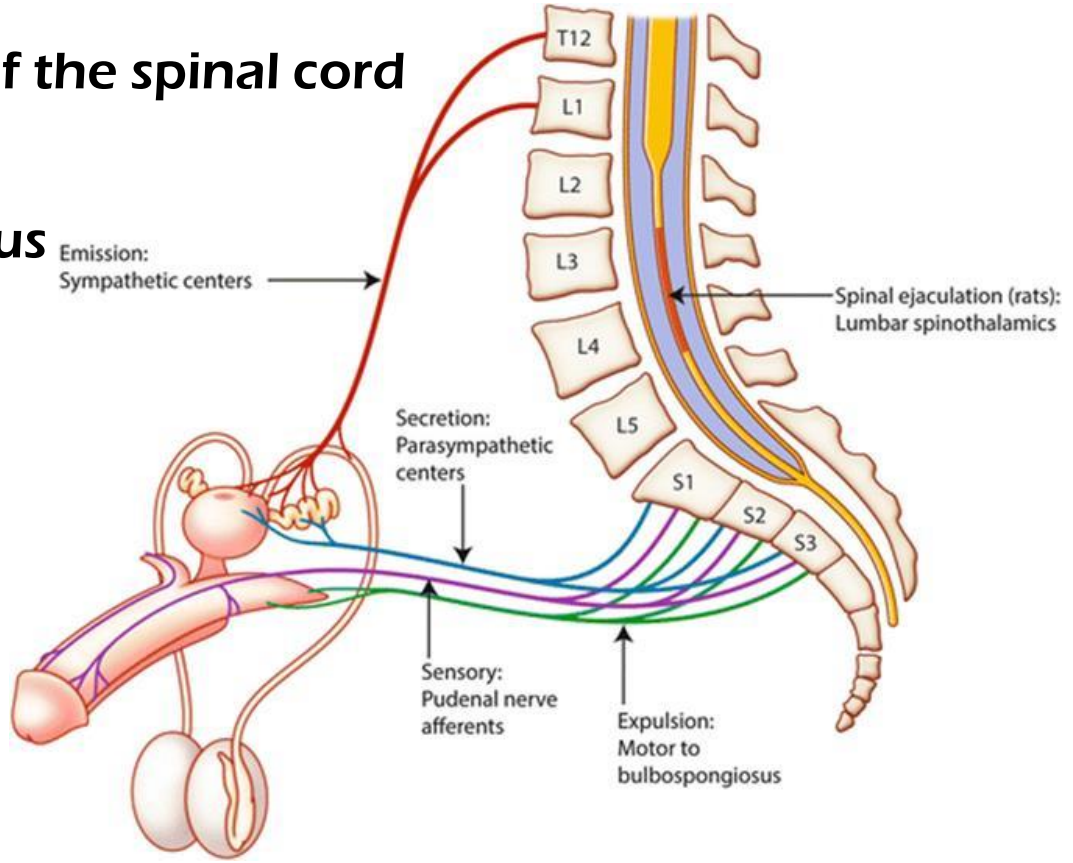
1. **Penile erection:**
   - Parasympathetic impulses from sacral portion of the spinal cord
2. **Lubrication:**
   - Urethral and bulbourethral glands secrete mucus by parasympathetic stimulation
3. **Emission and Ejaculation:**
   - Sympathetic nerve function from T_{12} to L_2

3-1- Emission:

- Contraction of vas deferens and ampulla cause expulsion of sperm
- Contraction of prostate and seminal vesicles expel their fluid
- Mucus secretes by bulbourethral gland to form semen

3-2- Ejaculation:

- Filling of internal urethra with semen sends impulse to sacral portion of spinal cord
- Rhythmical contraction of genital organs expel the semen to the outside of the body



Male Sex Hormones

- Androgens:
  - Testosterone: The most abundant androgen
  - Dihydrotestosterone: the active form of testosterone in the target tissues
  - Androstenedione
- Testosterone:
  - Is secreted by interstitial cells of Leydig
  - when the germinal epithelium of the testes is destroyed by x-ray treatment or excessive heat, the Leydig cells, which are less easily destroyed, often continue to produce testosterone.
  - Adrenal glands also secret androgens.
  - All androgens are steroid compounds.
  - Most of the testosterone is bound with sex hormone–binding globulin in the blood.

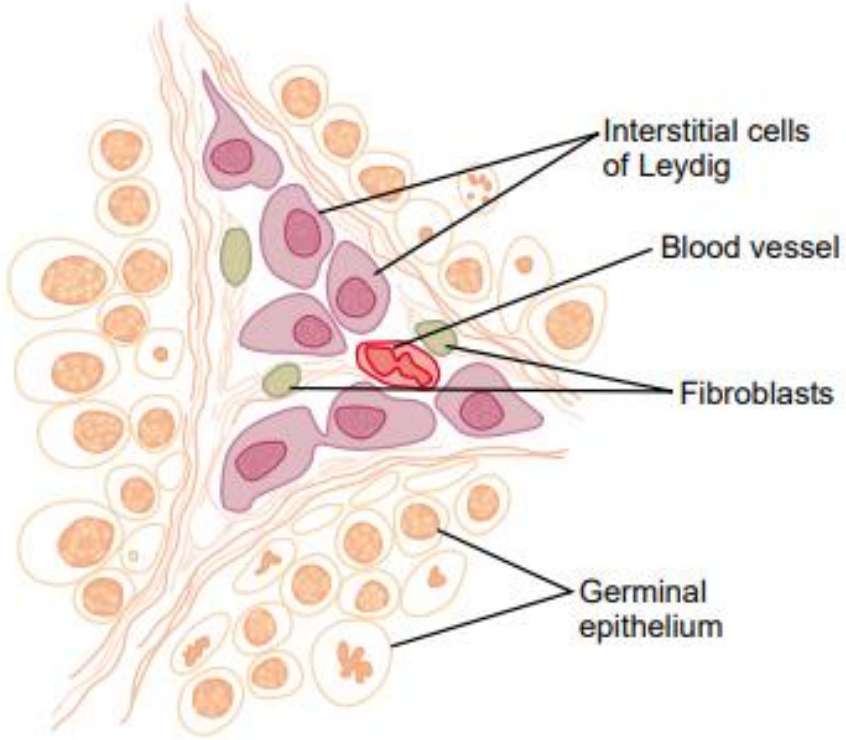
Functions of Testosterone

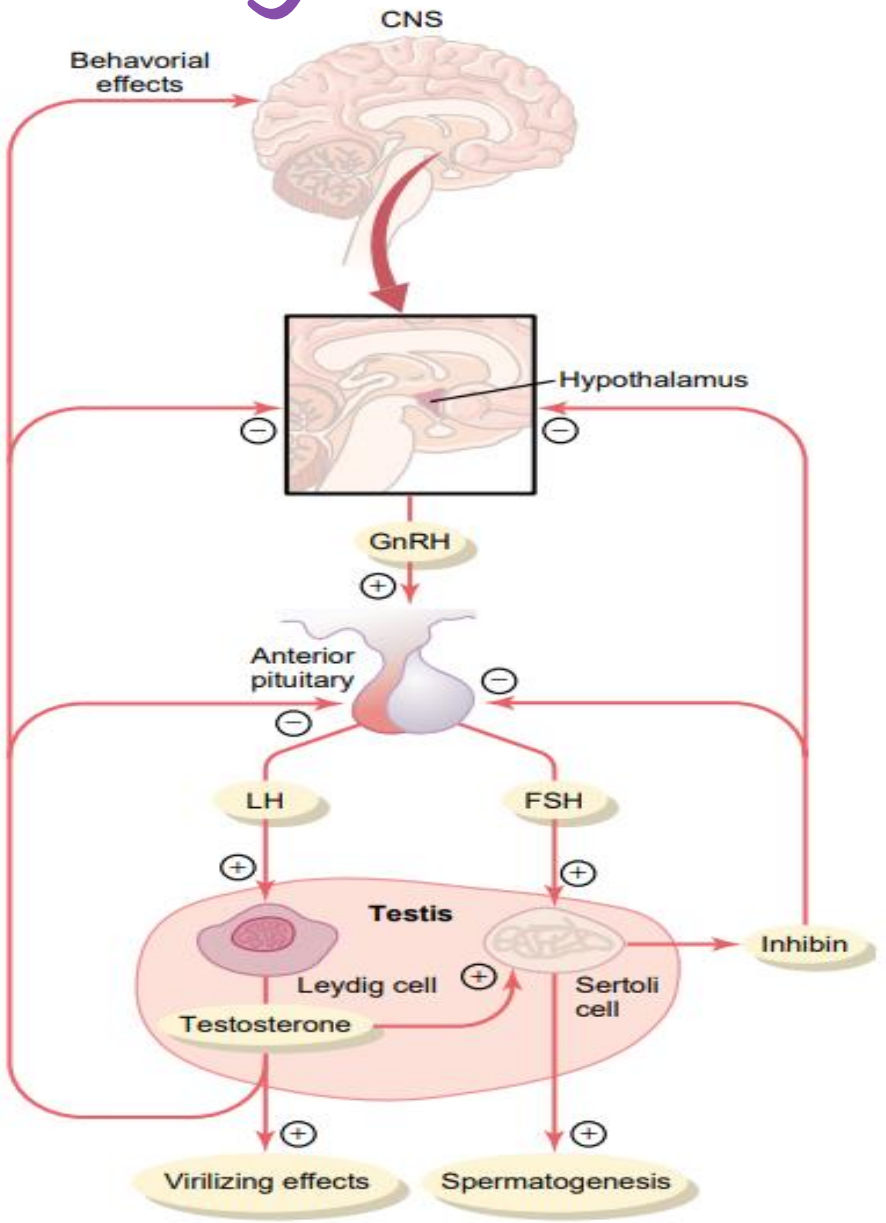
1. Testosterone secreted first by the genital ridges and later by the fetal testes (by the action of SR Y gene) is responsible for the development of the male body characteristics:
   - The formation of a penis and a scrotum rather than clitoris and a vagina.
   - formation of the prostate gland, seminal vesicles, and male genital ducts
2. Testicular descend into the scrotum during the last 2 to 3 months of gestation
3. Hair growth around pubis, chest, face, . . .
4. Decreases the growth of hair on the top of the head (genetic factor is needed for appearance of baldness).
5. Causes hypertrophy of the laryngeal mucosa and enlargement of the larynx
6. Increases the thickness of the skin over the entire body, excessively stimulate the sebaceous glands of the face, which leads to acne.

Functions of Testosterone

7. Increases musculature after puberty, averaging about a 50 per cent increase in muscle mass over that in the female.
8. Increases the total quantity of bone matrix and causes calcium retention.
9. Increases the basal metabolic rate by as much as 15 per cent.
10. Increases the number of red blood cells per cubic millimeter of blood by15 to 20 per cent.
11. Increase the reabsorption of sodium in the distal tubules of the kidneys.

Control of Male Sexual Functions by Hormones





Abnormalities of Male Sexual Function

Prostate Gland and Its Abnormalities

- The prostate gland remains relatively small throughout childhood and begins to grow at puberty under the stimulus of testosterone.
- This gland reaches an almost stationary size by the age of 20 years and remains at this size up to the age of about 50 years.
- A benign prostatic fibroadenoma frequently develops in the prostate in many older men and can cause urinary obstruction
- Cancer of the prostate gland can cause 2 to 3 per cent of all male deaths.
  - Testosterone can stimulate cancerous cells to more rapid growth
  - Removal of both testes and administration of estrogens can be successfully treat prostate cancer for a few months to years

Abnormalities of Male Sexual Function

Hypogonadism in the Male

- When the testes of a male fetus are nonfunctional during fetal life, none of the male sexual characteristics develop in the fetus. Instead, female organs are formed.
- The basic genetic characteristic of the fetus, whether male or female, is to form female sexual organs if there are no sex hormones.
- When a boy loses his testes before puberty, he continues to have infantile sex organs and other infantile sexual characteristics throughout life.

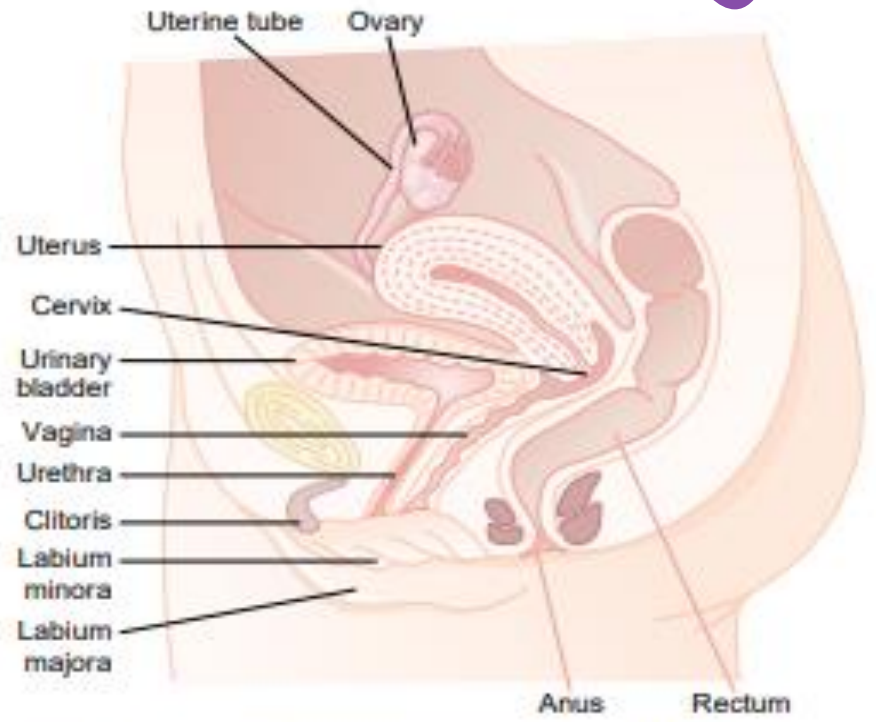
Testicular Tumors and Hypergonadism in the Male

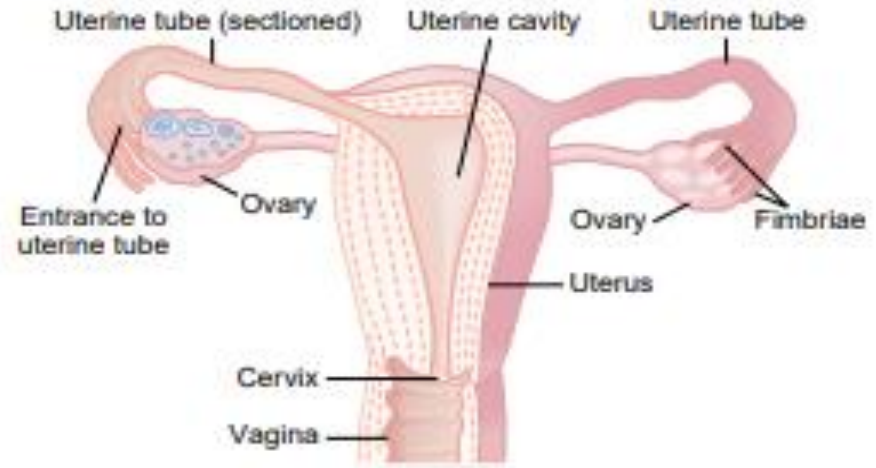
- Interstitial Leydig cell tumors develop in rare instances in the testes, but when they do develop, they sometimes produce as much as 100 times the normal quantities of testosterone.
  - Rapid growth of the musculature and bone
  - Early uniting of the epiphyses causes shorter height
  - Excessive development of the male sexual organs
- Tumors of the germinal epithelium are much more common
  - estrogenic hormones are sometimes secreted by these tumors and cause the condition called gynecomastia (overgrowth of the breasts).

Female Reproductive Physiology (Before Pregnancy)

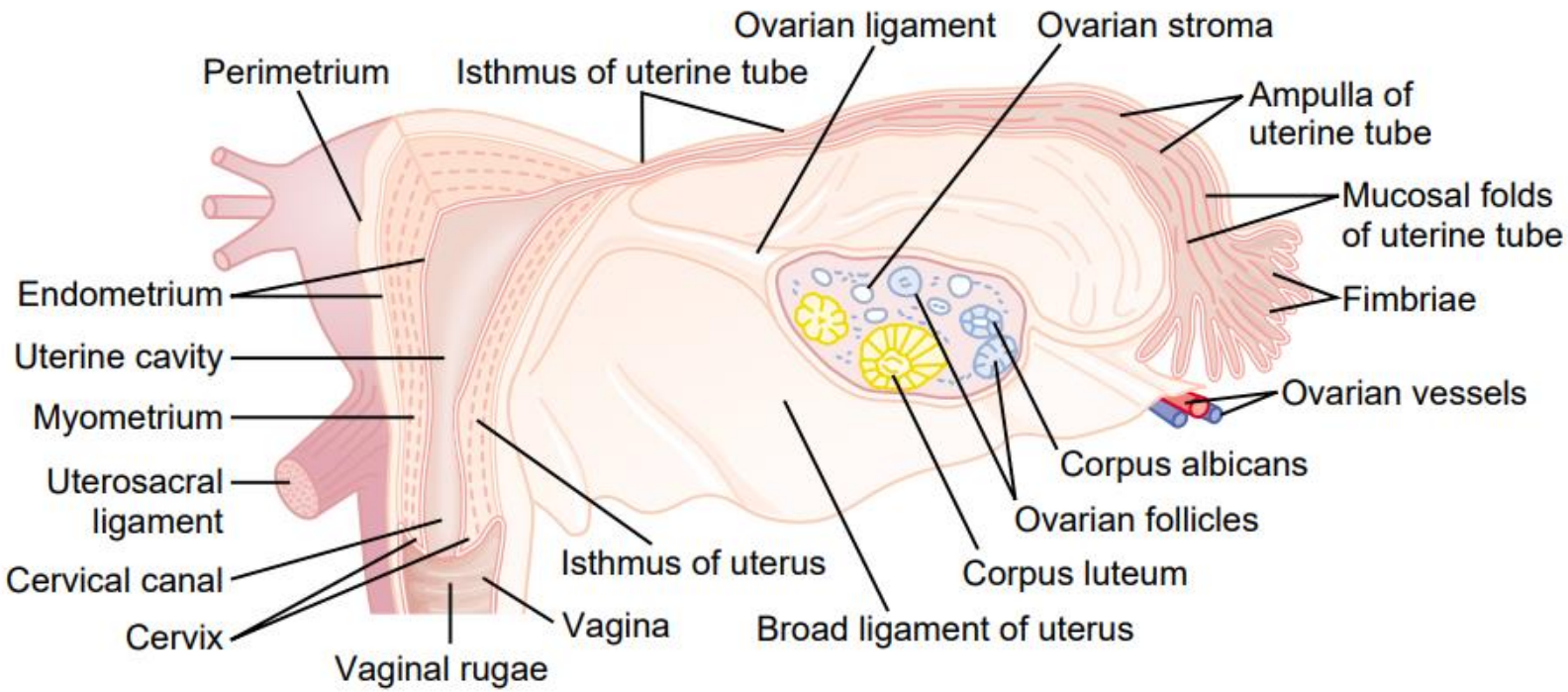
Physiologic Anatomy of the Female Sexual Organs

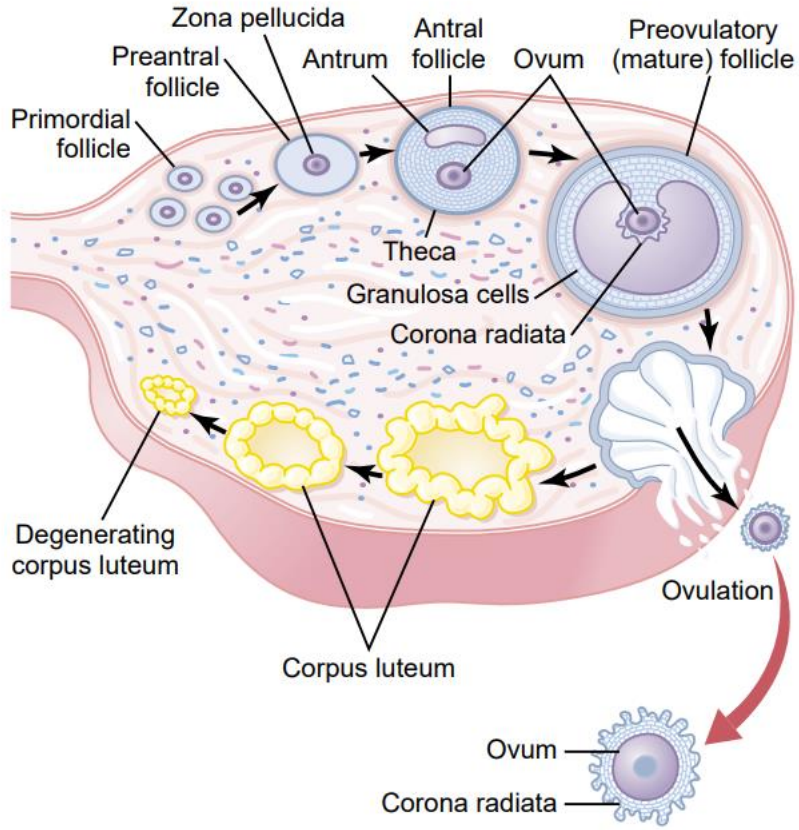
- Ovaries
  - Germinal epithelium
  - Stroma
- Uterine tube
  - Fimbriae
  - Isthmus
  - Ampulla
- Uterus
  - Endometrium
  - Myometrium
  - Perimetrium
- Cervix
- Vagina
- Clitoris





Physiologic Anatomy of the Female Sexual Organs

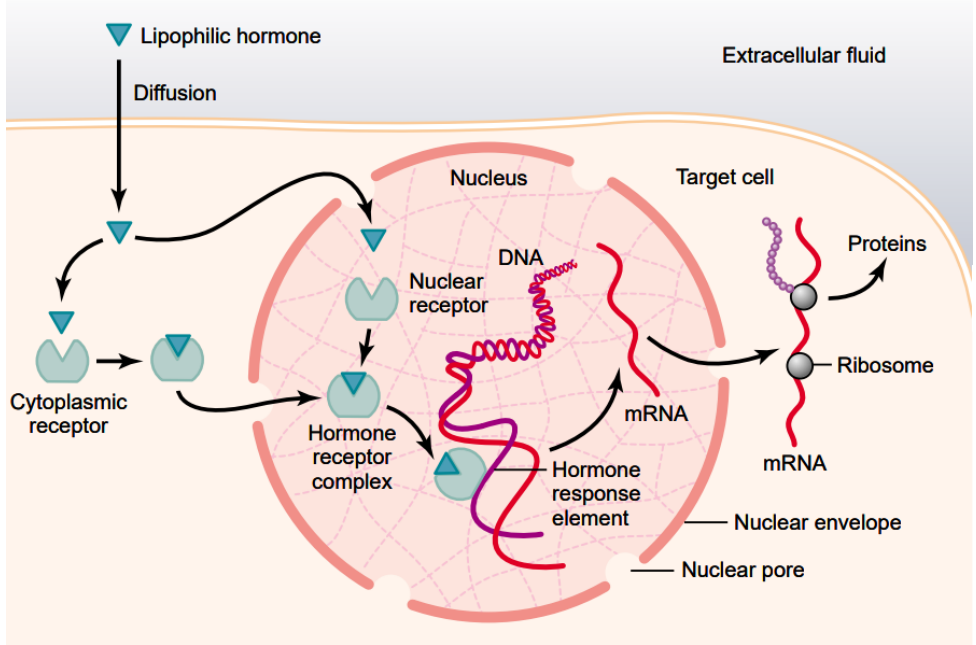




Functions of the Ovarian Hormones

- **Estrogens:**
  - **Estradiol** is the most important estrogen
  - Secreted by ovaries, adrenal cortex and placenta (during pregnancy)
- **Progestins:**
  - **Progesterone** is the most important progestins
  - Secreted by the corpus luteum and placenta (during pregnancy)

  - Both estrogens and progesterone are transported in the blood bound mainly with plasma albumin and with specific estrogen- and progesterone-binding globulins.
  - Lipophilic hormones, such as steroids bind with intracellular receptor on the DNA and activate or inhibit gene transcription.



Functions of the Estrogens

1. . . . on the Uterus and External Female Sex Organs

- The ovaries, fallopian tubes, uterus, and vagina all increase several times in size.
- The external genitalia enlarge, with deposition of fat in the mons pubis and labia majora and enlargement of the labia minora.
- Estrogens change the vaginal epithelium from a cuboidal into a stratified type
  - Cause more resistance to trauma and infection
  - Use for treatment of infants' vaginal infections

2. . . . on the Fallopian Tubes

- Proliferate the glandular tissue to secret more mucus
- Increase the activity of the cilia which always beat toward the uterus

3. . . . on the Breasts

- Development of the stromal tissues of the breasts
- Growth of an extensive ductile system
- Deposition of fat in the breasts

Functions of the Estrogens

4. . . . on Protein Deposition

- cause a slight increase in total body protein

5. . . . on the Skeleton

- Inhibit osteoclastic activity in the bones and therefore stimulate bone growth
- Cause uniting of the epiphyses with the shafts of the long bones much earlier than in males
- After menopause, almost no estrogens are secreted by the ovaries: Estrogen deficiency
  - Increase osteoclastic activity in the bones
  - decrease bone matrix
  - Decrease deposition of bone calcium and phosphate
  - Osteoporosis

6. . . . on Body Metabolism and Fat Deposition

- increase the whole-body metabolic rate slightly
- cause deposition of increased quantities of fat in the subcutaneous tissues
  - the percentage of body fat in the female body is considerably greater than that in the male body

Functions of the Estrogens

7. . . . on Hair Distribution

- do not greatly affect hair distribution. However, hair does develop in the pubic region and in the axillae after puberty

8. . . . on the Skin

- Cause the skin soft and smooth, but thicker than that of a child or a castrated female
- Cause the skin to become more vascular, so s greater bleeding of cut surfaces than is observed in men

9. . . . on Electrolyte Balance

- Cause sodium and water retention by the kidney tubules slightly.
- During pregnancy, the tremendous formation of estrogens by the placenta may contribute to body fluid retention

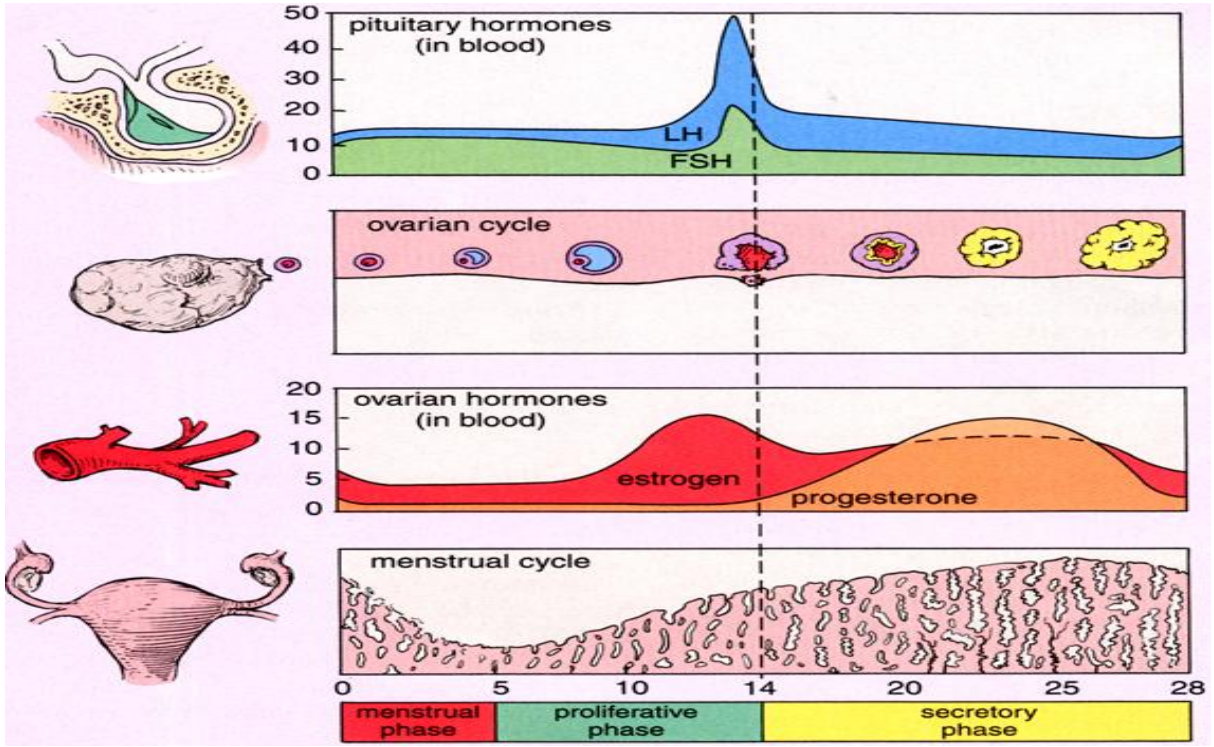
Functions of Progesterone

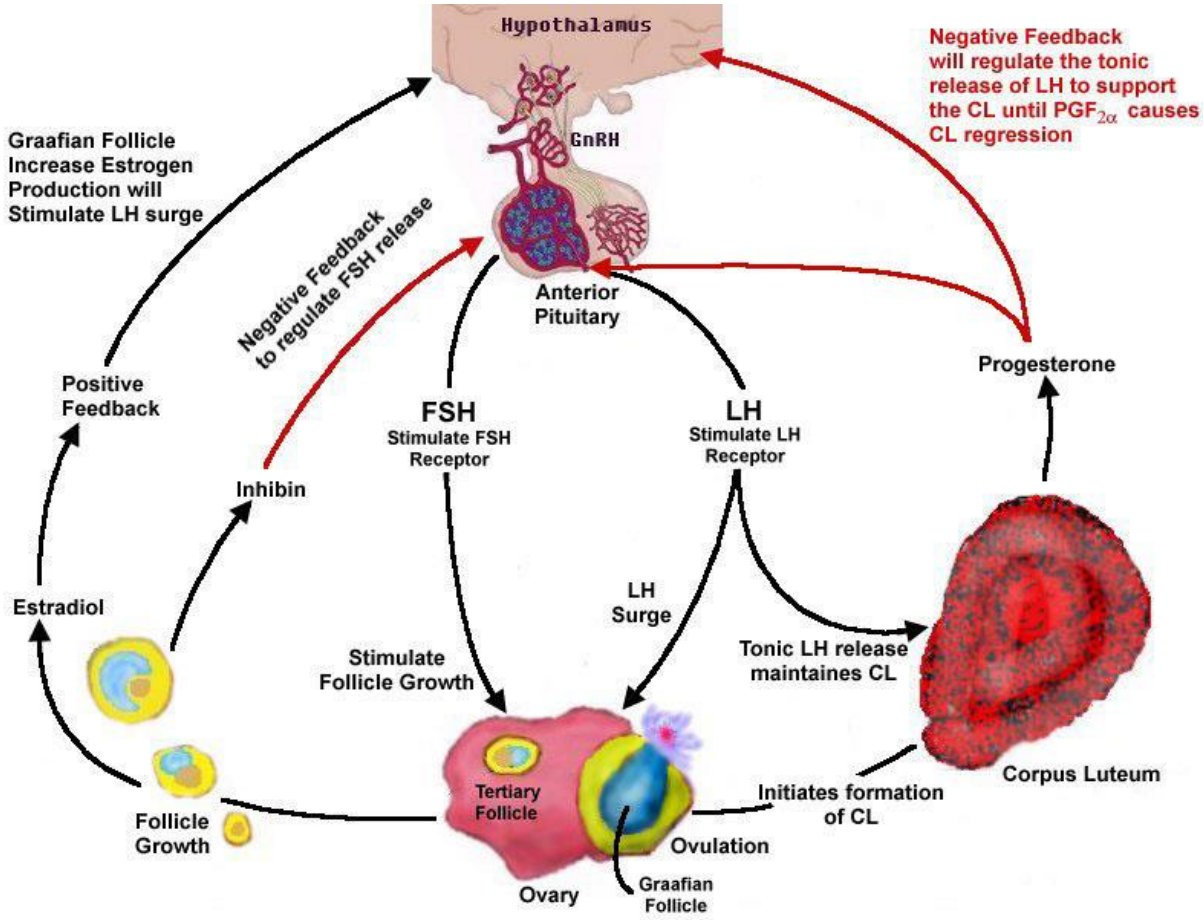
1. . . . on the Uterus
   - Promote secretory changes in the uterine endometrium during the luteal phase of the menstrual cycle
   - Decreases the frequency and intensity of uterine contractions

2. . . . on the Fallopian Tubes
   - Promotes increased secretion by the mucosal lining of the fallopian tubes

3. . . . on the Breasts
   - Promotes development of the lobules and alveoli of the breasts, causing the alveolar cells to proliferate, enlarge, and become secretory in nature

Monthly Ovarian Cycle





Monthly Endometrial Cycle and Menstruation

- **Proliferative Phase (Estrogen Phase):**
  - After menstruation, under the influence of estrogens, secreted in increasing quantities by the ovary, the stromal cells and the epithelial cells proliferate rapidly.
  - During the next week and a half the endometrium increases greatly in thickness
  - At the time of ovulation, the endometrium is 3 to 5mm thick
  - The endometrial glands, especially those of the cervical region, secrete a thin, stringy mucus
  - The mucus around cervix form channels that help guide sperm in the proper direction from the vagina into the uterus
- **Secretory Phase (Progestational Phase):**
  - During most of the 2nd half of the monthly cycle, after ovulation has occurred, progesterone and estrogen are secreted in large quantities by the corpus luteum.
    - The estrogens cause slight additional cellular proliferation in the endometrium
    - Progesterone causes marked swelling and secretory development of the endometrium
    - The uterine secretions, called "uterine milk," provide nutrition for the early dividing ovum

The Menstrual Cycle

The Menstrual Cycle

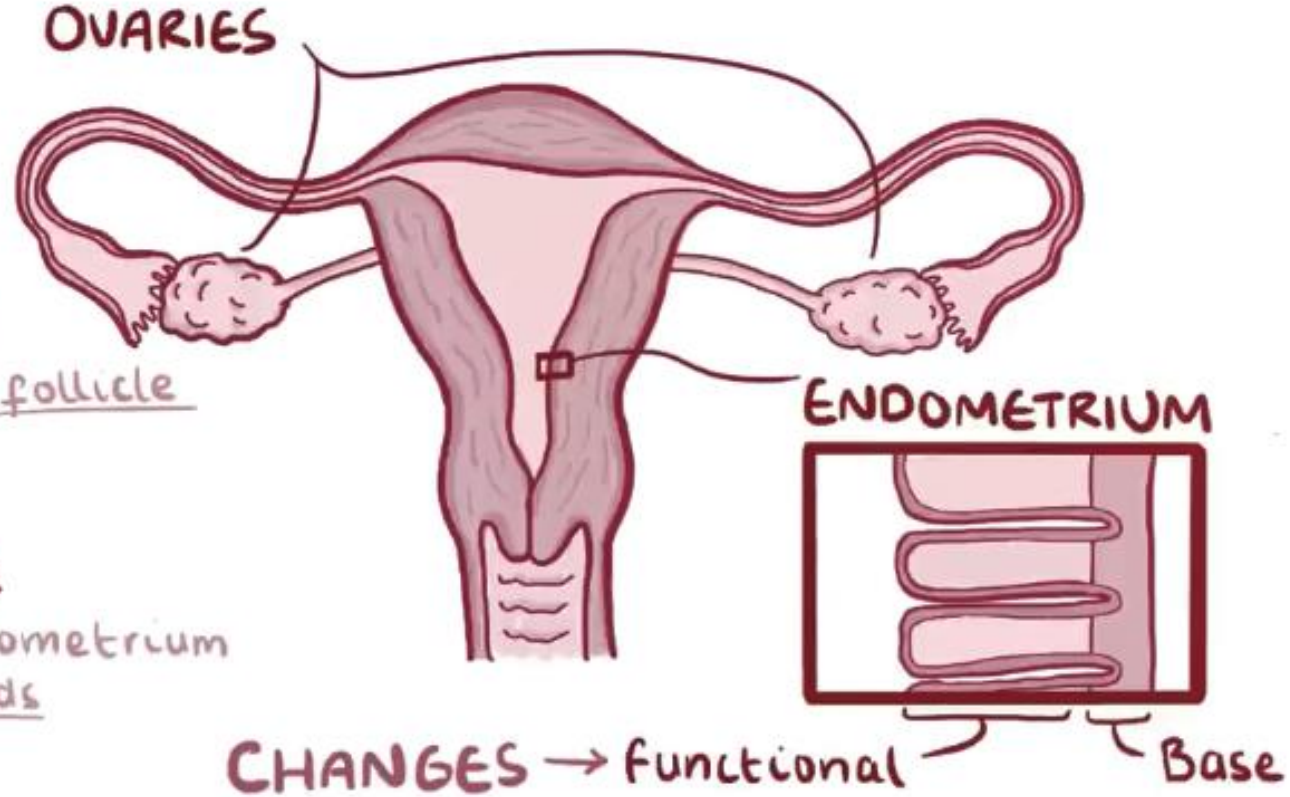
THE MENSTRUAL CYCLE

MAKES REPRODUCTION POSSIBLE

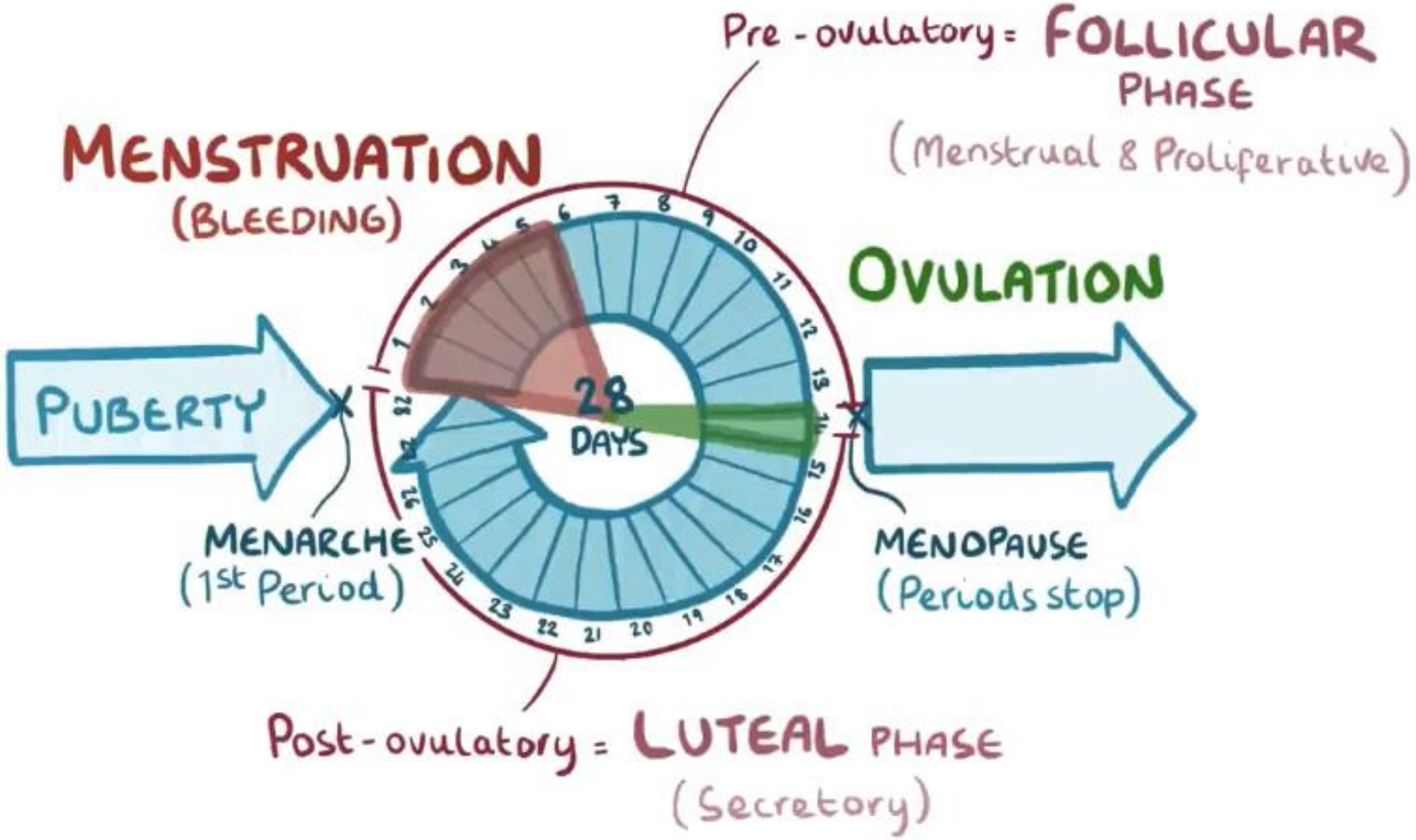
2 SYNCHRONIZED ENTITIES

① OVARIAN CYCLE
- Development of follicle
- Ovulation

② UTERINE CYCLE
- Functional endometrium thickens & sheds



The Menstrual Cycle



The Menstrual Cycle

FOLLICULAR PHASE

* 1st day of menstruation
* Weeks 1 & 2 of 4-week cycle

MASTERMINDS

HYPOTHALAMUS

ANTERIOR PITUITARY

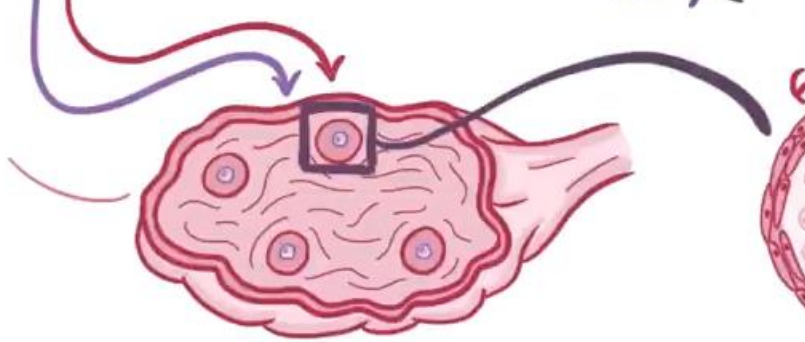
GONADOTROPIN-RELEASING HORMONE (GnRH) – After puberty, released in **PULSES**

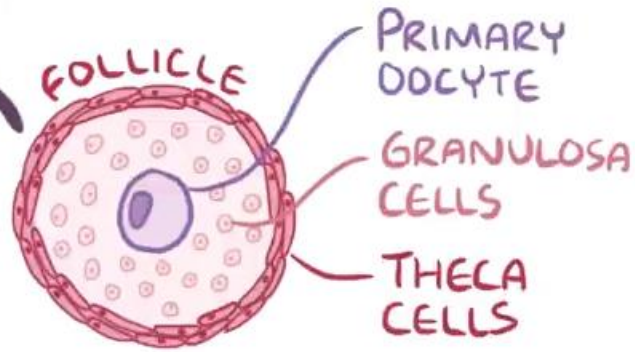
Determines amount of

FOLLICLE STIMULATING HORMONE (FSH)

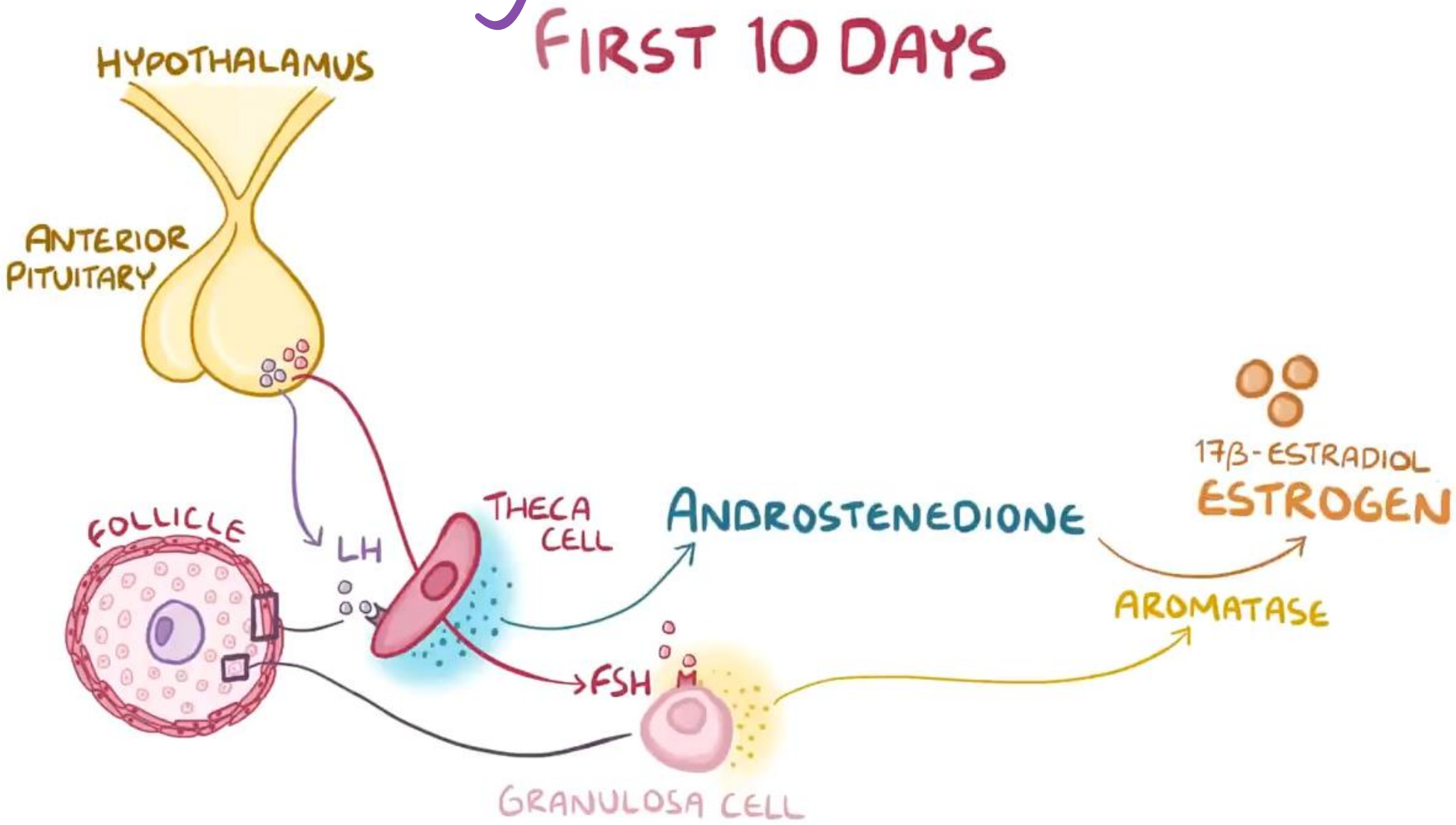
LUTEINIZING HORMONE (LH)

Ovarian follicles compete to grow **FASTEST**

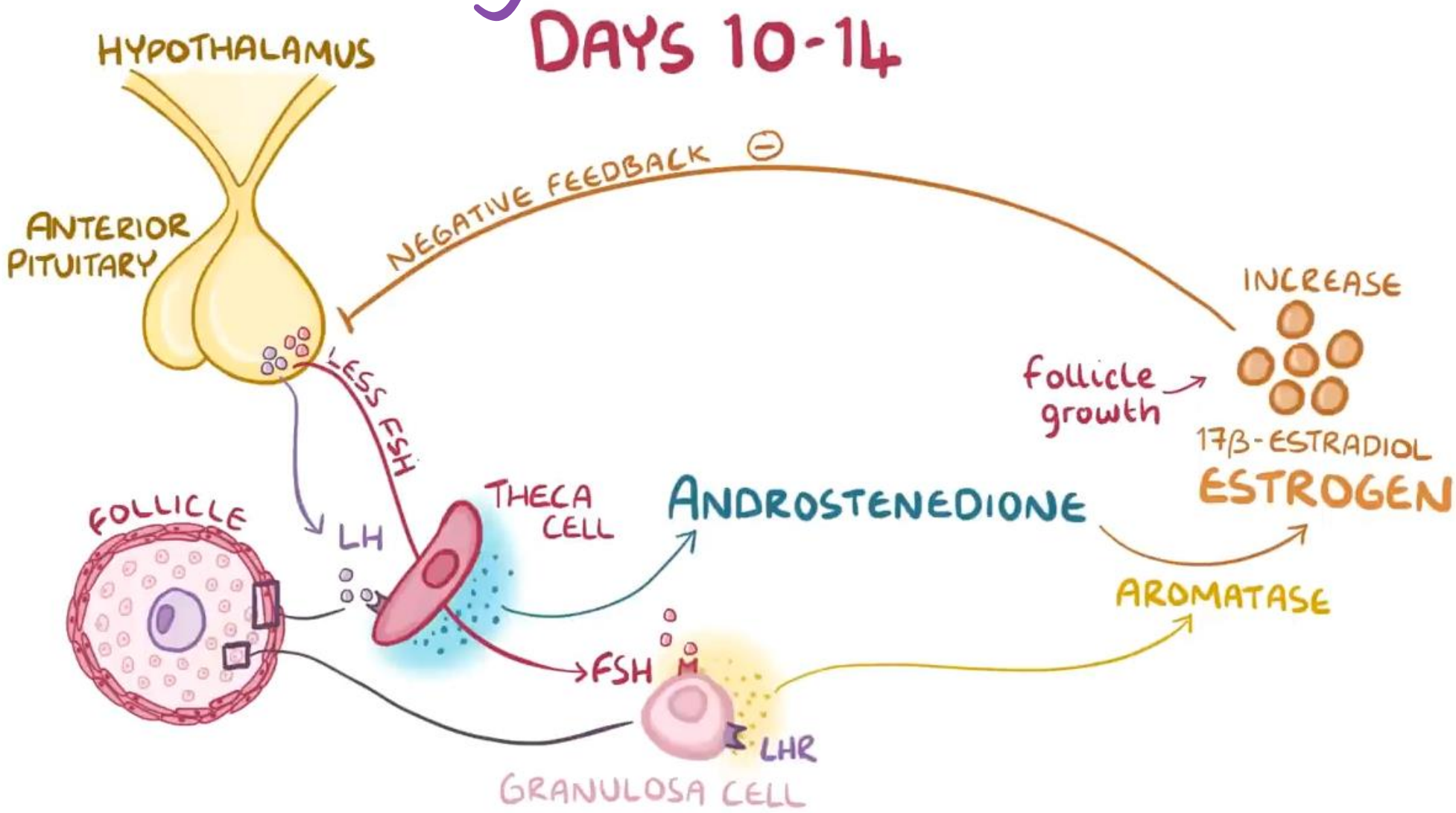




The Menstrual Cycle

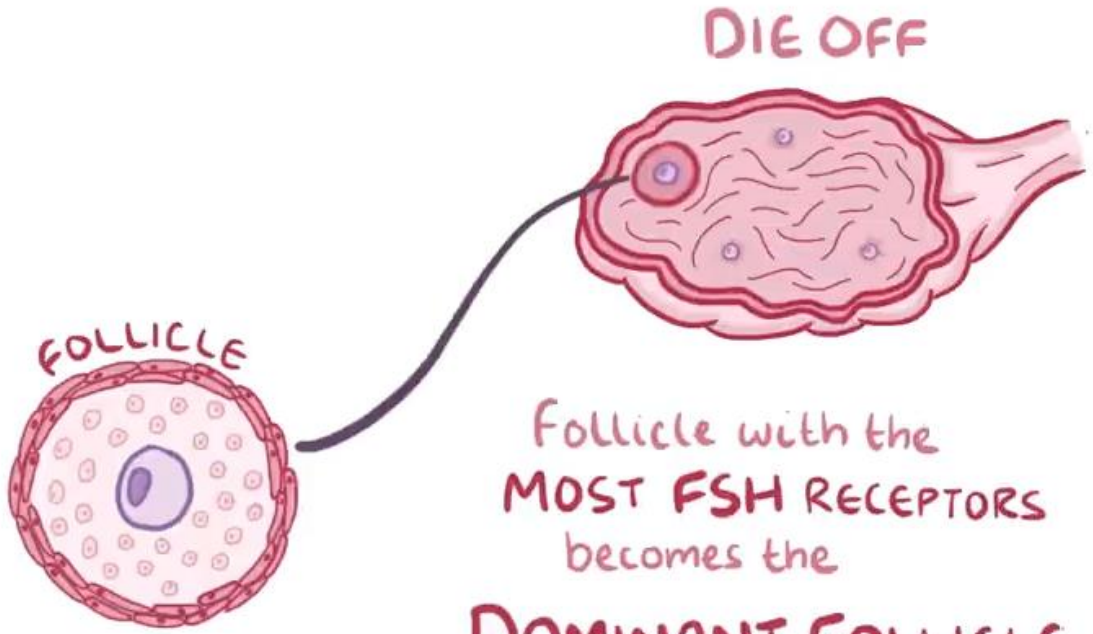


The Menstrual Cycle

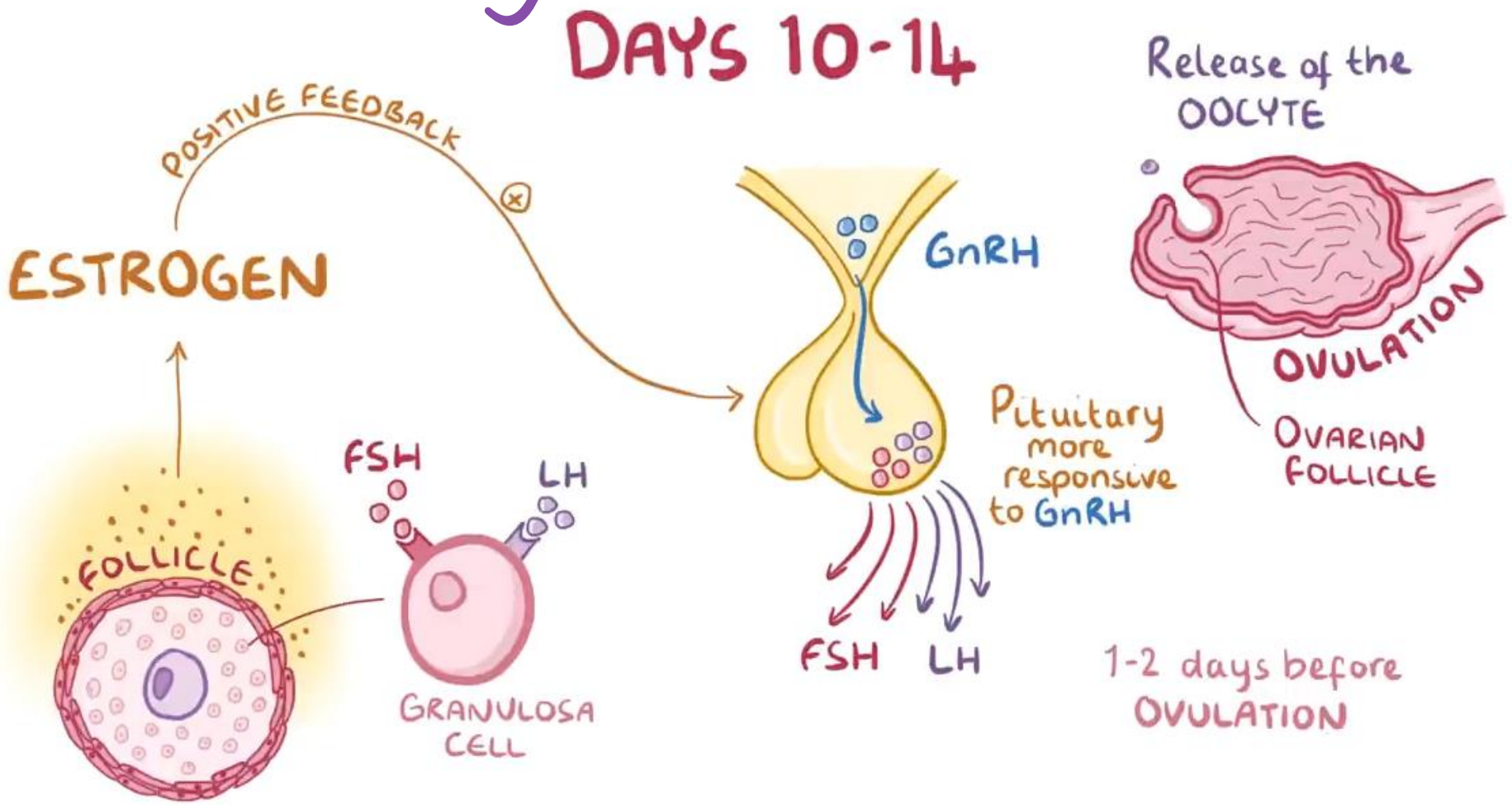


The Menstrual Cycle

DAYS 10-14

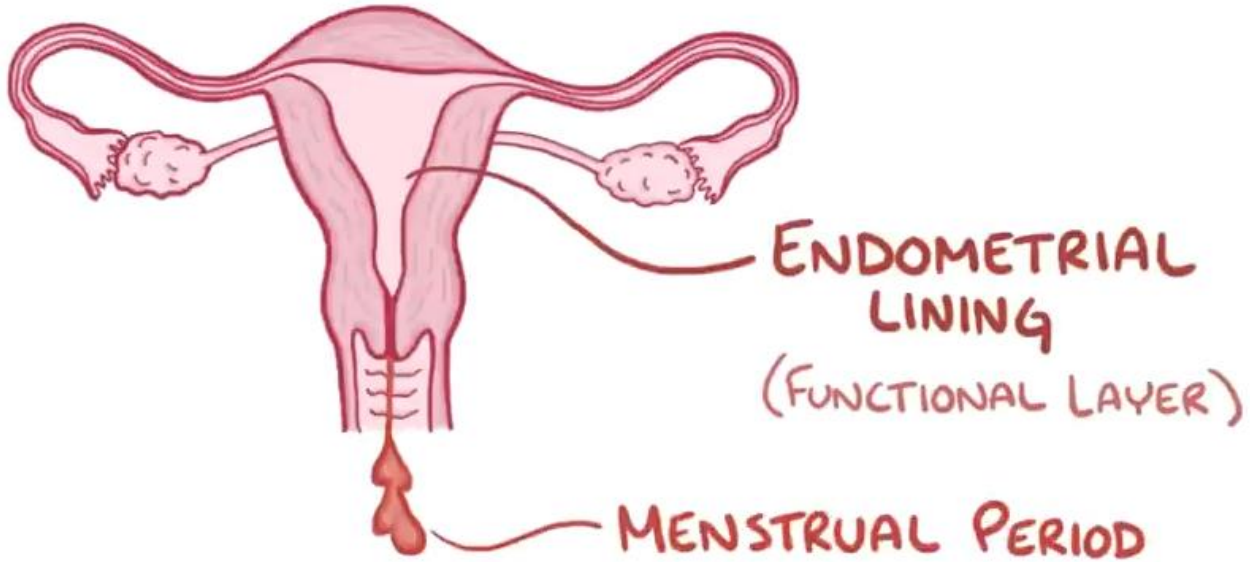


The Menstrual Cycle



The Menstrual Cycle

Menstrual Phase



The Menstrual Cycle

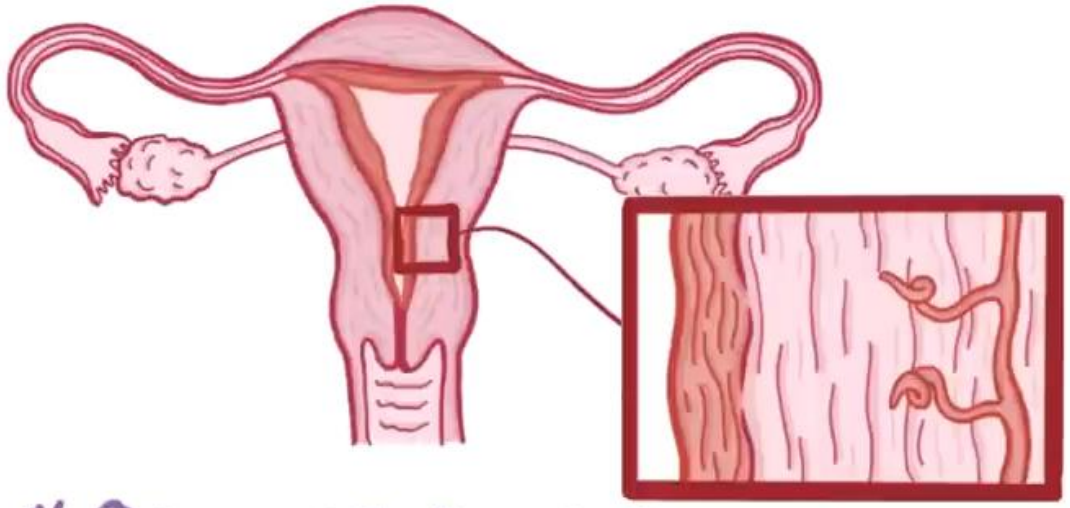
Proliferative Phase

* ↑ Estrogen Levels

~ Thickening of Endometrium

~ Growth of Endometrial Glands

~ Emergence of Spiral Arteries

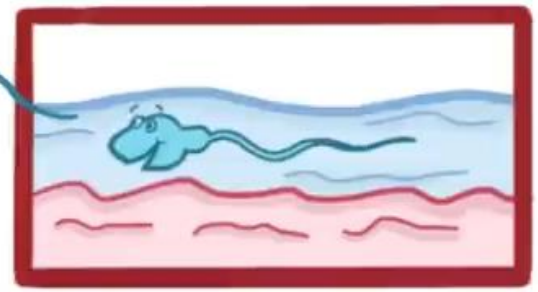


* Optimize Chance for Fertilization

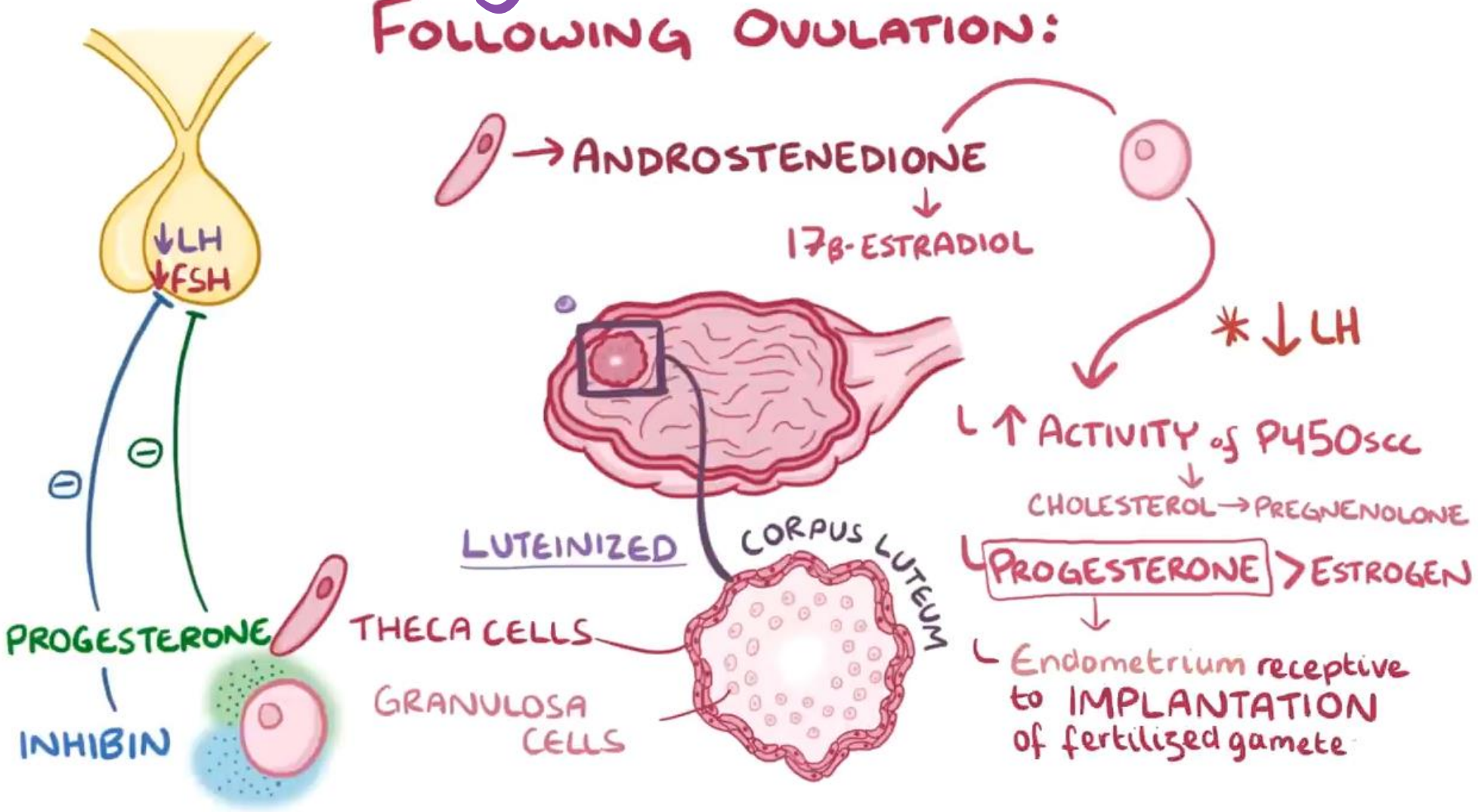
Day 11 + Day 15

Cervical Mucus

↳ More Hospitable for Sperm



The Menstrual Cycle

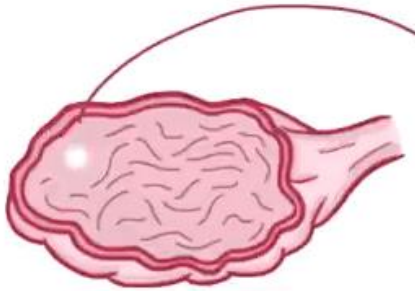


The Menstrual Cycle

UTERUS GOES THROUGH **SECRETORY PHASE**

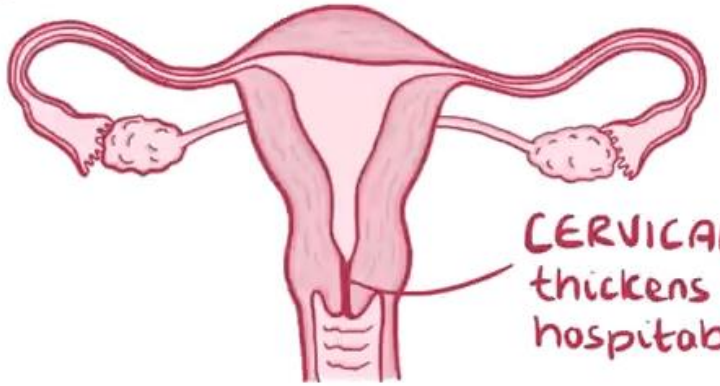
- SPIRAL ARTERIES grow longer
- Uterine glands secrete more mucus

AFTER DAY 15 – Window for fertilization starts to close



CORPUS LUTEUM replaced by **CORPUS ALBICANS**

Doesn't make hormones



CERVICAL MUCUS thickens – less hospitable for SPERM

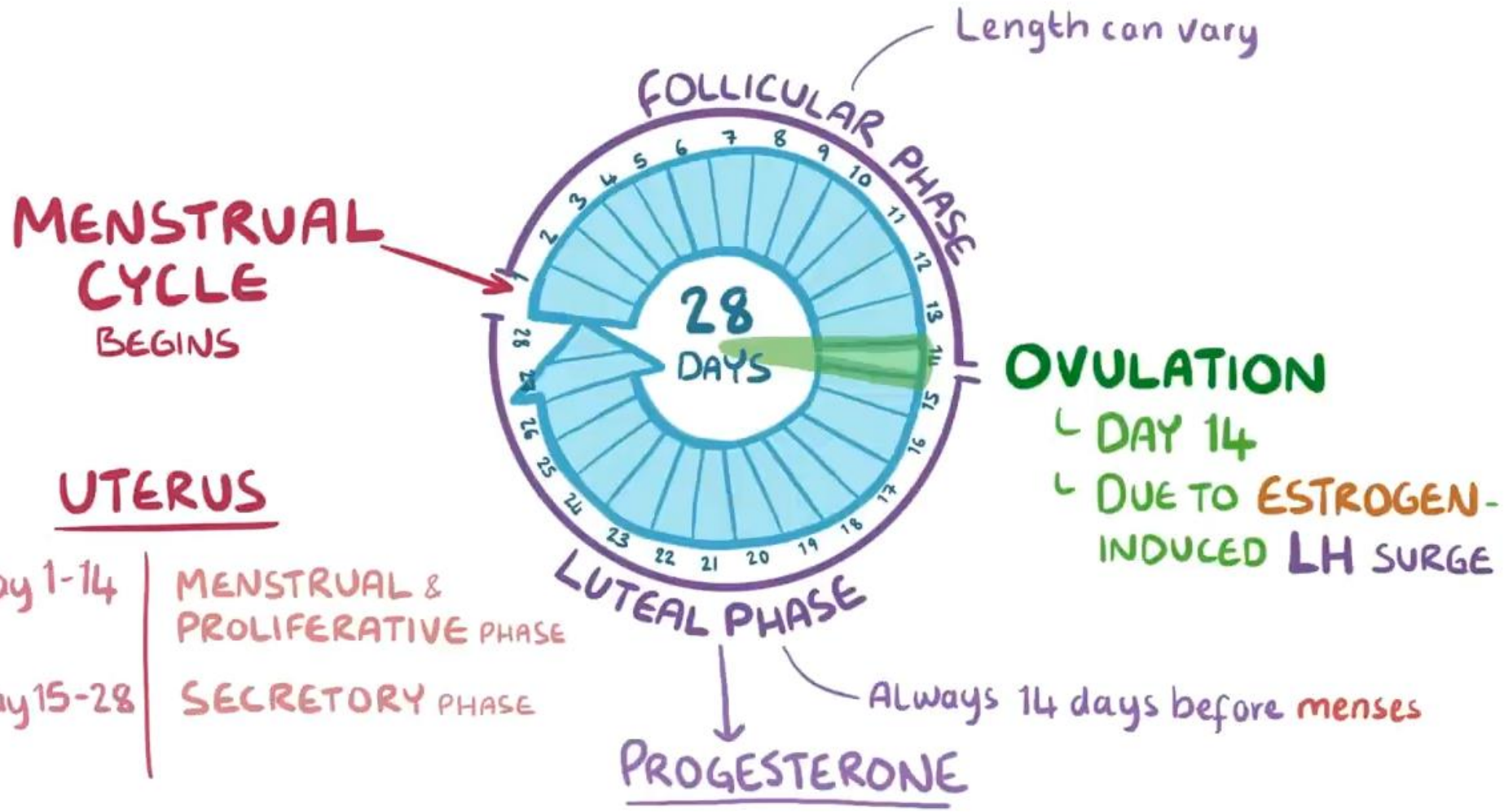
↓ESTROGEN

↓PROGESTERONE – At lowest:

- SPIRAL ARTERIES collapse
- Functional layer sloughs off – MENSTRUATION

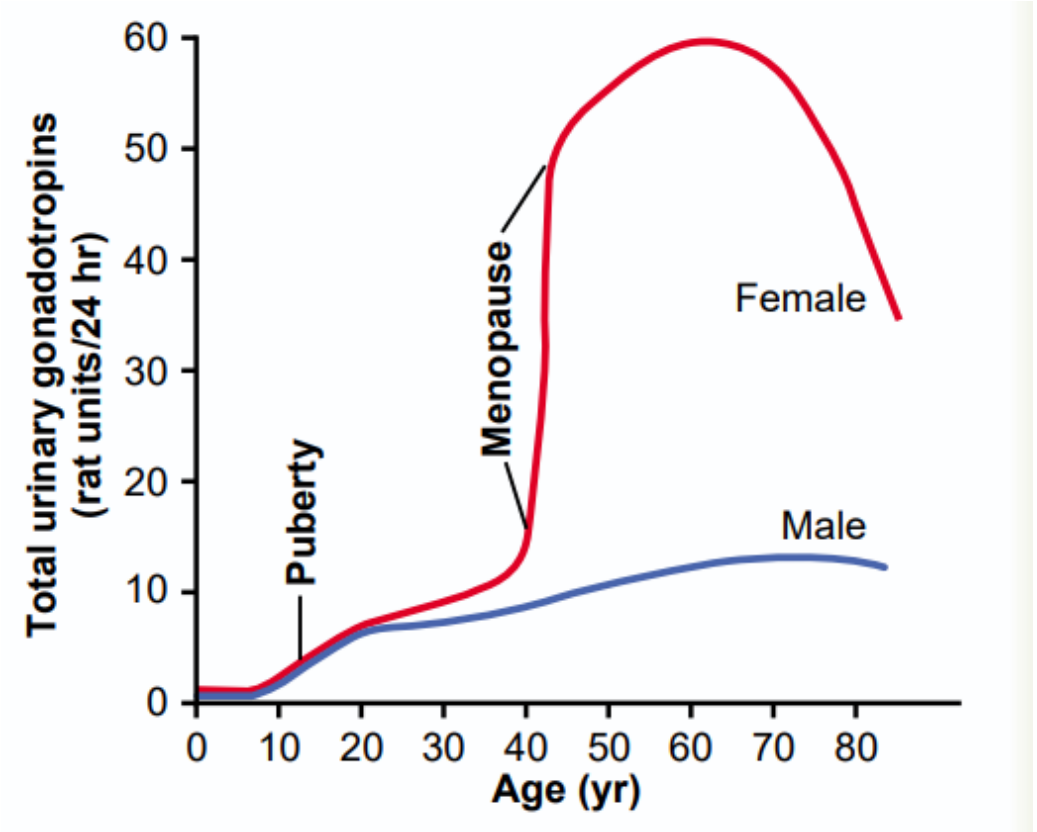
NEW MENSTRUAL CYCLE

The Menstrual Cycle



Puberty and Menarche

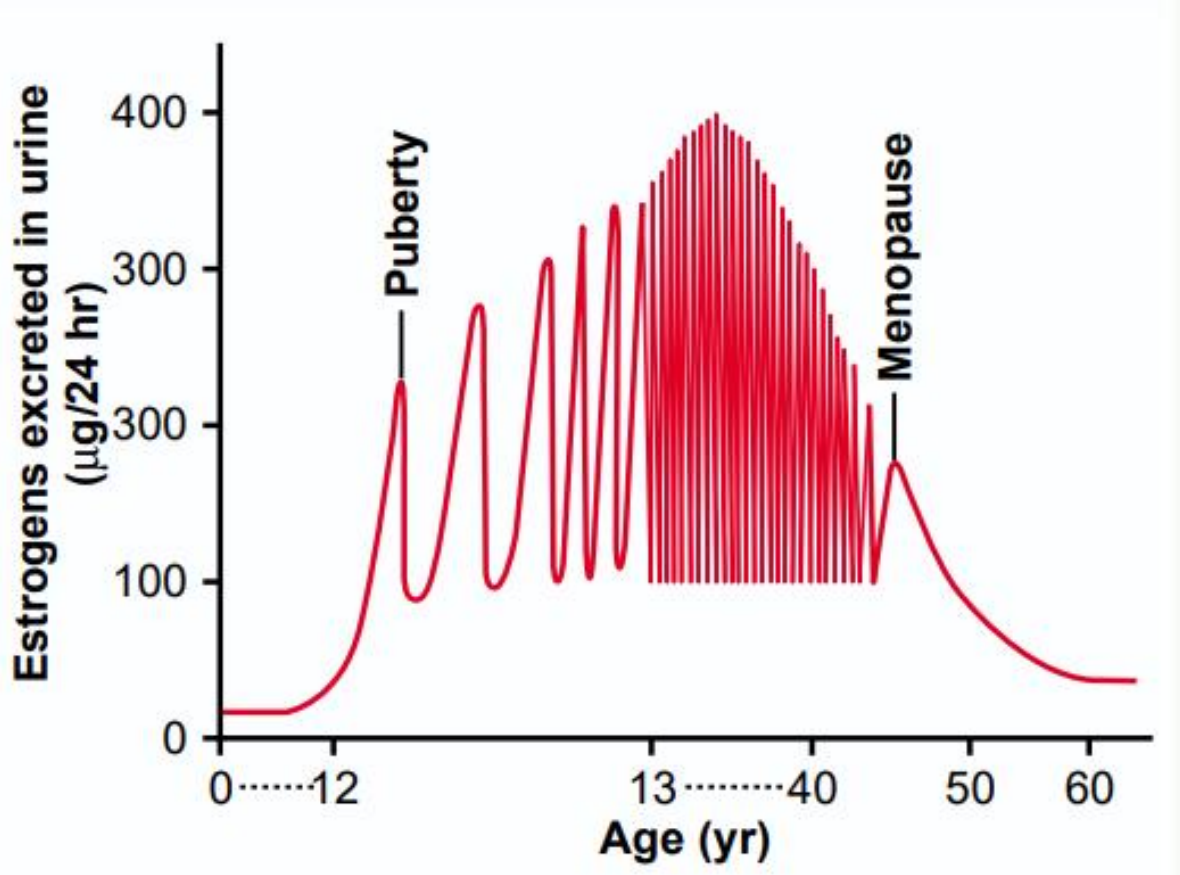
- **Puberty**: the onset of adult sexual life
  - The period of puberty is caused by a gradual increase in gonadotropic hormone secretion by the pituitary, beginning in about the eighth year of life
  - Usually, the onset of puberty and menstruation is between ages 11 and 16 years in girls (average, 13 years)
  - the hypothalamus does not secrete significant quantities of GnRH during childhood
  - The onset of puberty is initiated by some maturation process that occurs elsewhere in the brain, perhaps somewhere in the limbic system.
- **Menarche**: the beginning of the cycle of menstruation



Puberty and Menarche

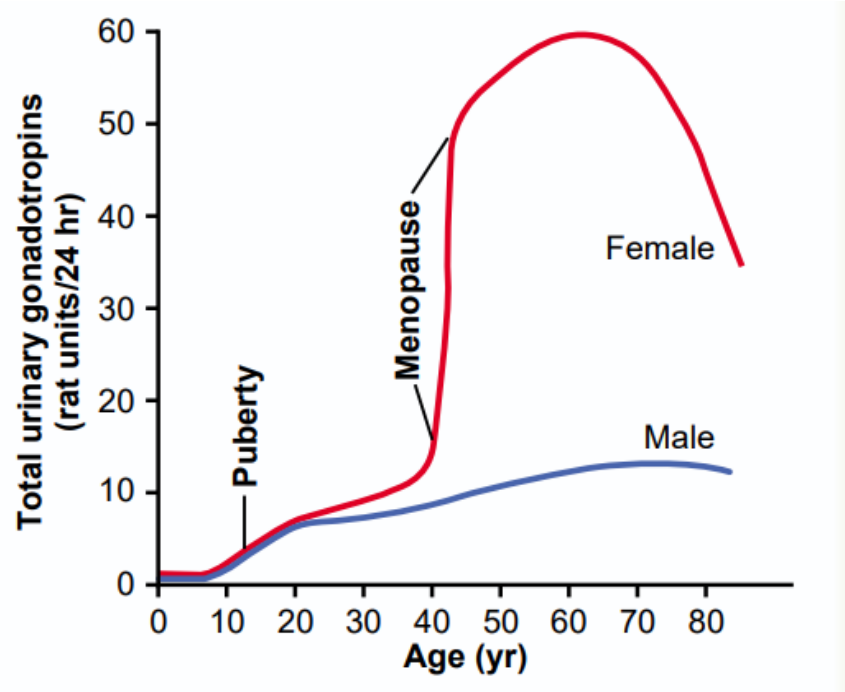
Estrogen secretion throughout sexual life of a female:

- The increasing levels of estrogen secretion at puberty
- The cyclical variation during the monthly sexual cycle
- The further increase in estrogen secretion during the first few years of reproductive life
- The progressive decrease in estrogen secretion toward the end of reproductive life
- Almost no estrogen or progesterone secretion beyond menopause.



Menopause

- The period during which the cycle ceases and the female sex hormones diminish to almost none is called menopause.
  - At age 40 to 50 years, the sexual cycle usually becomes irregular, and ovulation often fails to occur
- The production of estrogens by the ovaries decreases as the number of primordial follicles approaches zero.
  - When estrogen production falls below a critical value, the estrogens can no longer inhibit the production of the gonadotropins FSH and LH.
  - Therefore, FSH and LH (mainly FSH) are produced after menopause in large and continuous quantities, but as the remaining primordial follicles become atretic, the production of estrogens by the ovaries falls virtually to zero

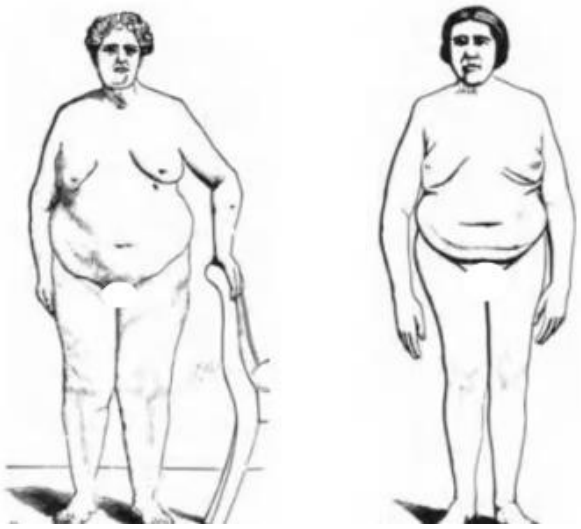


Menopause

- The loss of estrogens often causes marked physiological changes in the function of the body:
  - "hot flushes" characterized by extreme flushing of the skin,
  - Psychic sensations of dyspnea
  - Irritability
  - Fatigue
  - Anxiety
  - Occasionally various psychotic states
  - Decreased strength and calcification of bones throughout the body
- In about 15 per cent of women, these symptoms need treatment
  - If counseling fails, daily administration of estrogen in small quantities usually reverses the symptoms, and by gradually decreasing the dose, postmenopausal women can likely avoid severe symptoms.

Abnormalities of Secretion by the Ovaries

- **Hypogonadism:**
- Caused by: poorly formed ovaries, lack of ovaries, or genetically abnormal ovaries
- Female eunuchism
  - prolonged growth of the long bones
  - the uterus becomes almost infantile in size
  - The vagina becomes smaller, and the vaginal epithelium becomes thin and easily damaged
  - The breasts atrophy and become pendulous
  - the pubic hair becomes thinner
  - The same changes occur in women after menopause



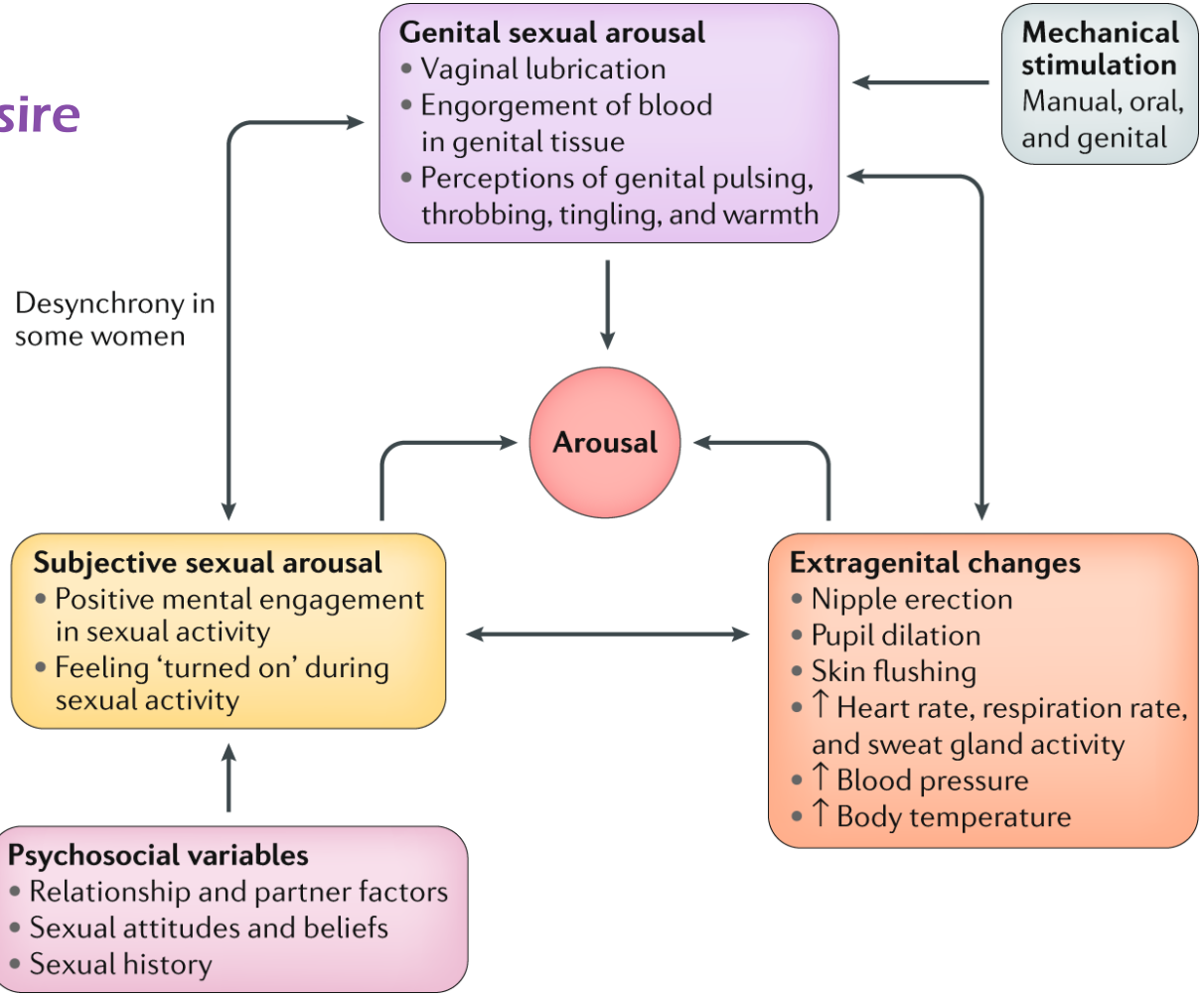
- Irregularity of Menses, and Amenorrhea (stopping menstruation) can also caused by hypothyroidism which leads to hypogonadism
- Prolonged ovarian cycles are frequently associated with failure of ovulation because of insufficient LH secretion

Abnormalities of Secretion by the Ovaries

- **Hypersecretion by the Ovaries**:
- Is a rare clinical symptom, because excessive secretion of estrogens automatically inhibits the pituitary, and this limits the production of ovarian hormones
- Usually happens when a feminizing tumor develops
  - A rare granulosa cell tumor can develop in an ovary, occurring more often after menopause than before
  - Bleeding is often the first and only indication that such a tumor exists

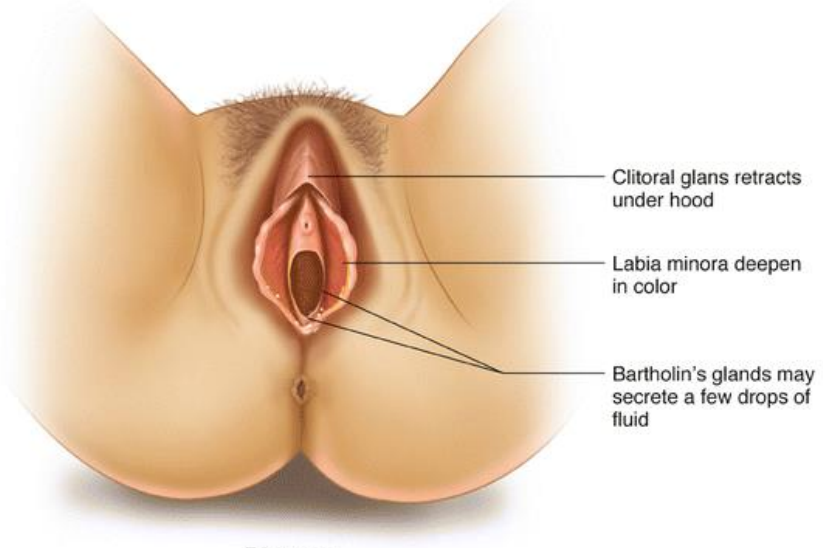
Female Sexual Act

- **Stimulation of the Female Sexual Act**
- **Psychic stimulation:**
  - Thinking sexual thoughts → sexual desire (based on woman's background training)
  - Sexual desire does increase in proportion to the level of sex hormones secreted
  - Desire also changes during the monthly sexual cycle, reaching a peak near the time of ovulation (high levels of estrogens)
- **Local sexual stimulation:**
  - stimulation of the vulva, vagina, and other perineal regions
  - The glans of the clitoris is especially sensitive for initiating sexual sensation
  - sexual sensory signals are transmitted to the sacral segments of the spinal cord then transmitted to the cerebrum

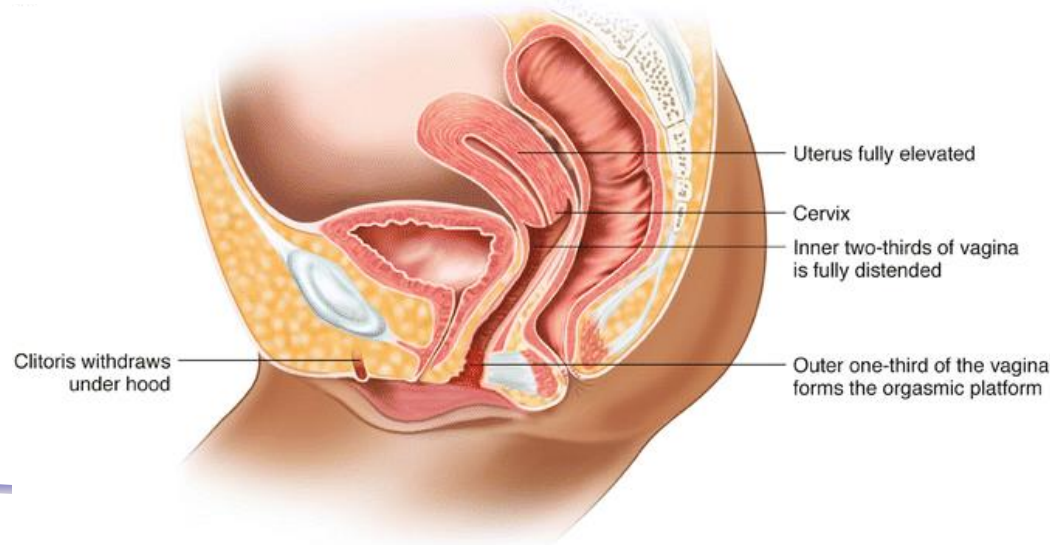


Female Sexual Act

- **Female erection and lubrication**
- There is erectile tissue at the entrance of vagina and clitoris almost identical to the erectile tissue of the penis
  - It is controlled by the parasympathetic nerves from the sacral plexus to the external genitalia
  - Release of acetylcholine (Ach), nitric oxide (NO), and vasoactive intestinal polypeptide (VIP) at the nerve endings dilate the arteries of erectile tissue
- Parasympathetic signals also pass to the bilateral Bartholin's glands located beneath the labia minora and cause them to secrete mucus immediately inside the vaginal entrance



Plateau



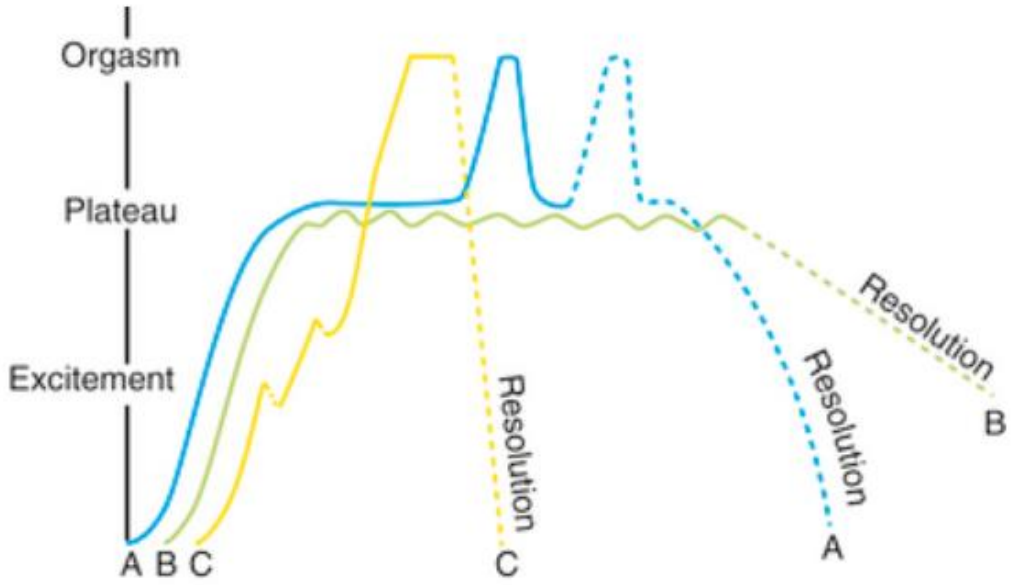
Plateau phase

Female Sexual Act

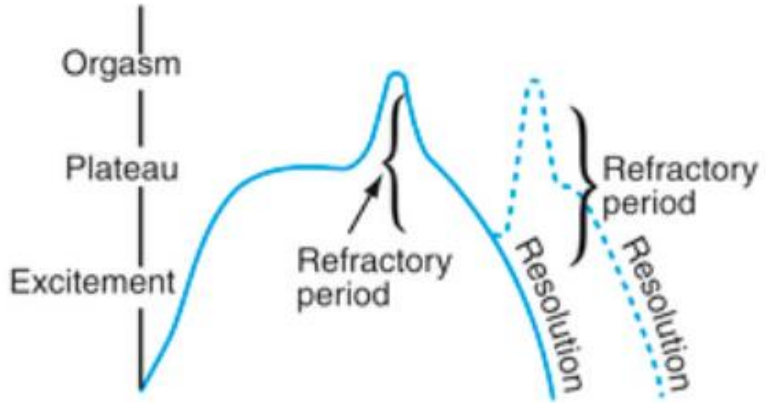
- **Female Orgasm**
- When local sexual stimulation reaches maximum intensity, especially supported by appropriate psychic signals from the cerebrum, reflexes are initiated that cause the female orgasm, also called the female climax
  - It is analogous to emission and ejaculation in the male and it may help promote fertilization of the ovum
- The human female is known to be more fertile when inseminated by normal sexual intercourse rather than by artificial methods
  - During the orgasm, the perineal muscles of the female contract rhythmically, that cause ejaculation in the male
  - These reflexes increase uterine and fallopian tube motility during the orgasm, thus helping to transport the sperm upward through the uterus toward the ovum
  - The orgasm seems to cause dilation of the cervical canal for up to 30 minutes

Human Sexual Response Cycle

- Masters and Johnson first described the physiology of "human sexual response cycle" in 1966
  - Excitement, Plateau, Orgasm, and Resolution
- Desire precedes both cycles in this model.
  - The length of the plateau phase is variable.
  - Women may have a brief plateau followed by orgasm (cycle C)
  - or a long plateau with no orgasm (cycle B).
  - Women may have multiple orgasms before resolution, although many do not (cycle A).
  - For men with premature ejaculation, the plateau phase is brief.
  - After ejaculation, men enter a refractory period lasting minutes to hours during which they are unable to ejaculate.



Female



Male

Female Orgasm

Female Fertility

- **Fertile Period of Each Sexual Cycle:**
- The ovum remains viable and capable of being fertilized for about 24 hours
  - A few sperm can remain fertile in the female genital tract for up to 5 days
  - Therefore, intercourse must occur sometime between 4 and 5 days before ovulation up to a few hours after ovulation
- **Rhythm Method of Contraception:**
- One of the commonly practiced methods of contraception is to avoid intercourse near the time of ovulation
  - the interval from ovulation until the next succeeding onset of menstruation is almost always between 13 and 15 days
  - Therefore, if the menstrual cycle is regular, with an exact periodicity of 28 days, ovulation usually occurs within 1 day of the 14^{th} day of the cycle
  - If the cycle takes 40 days, ovulation usually occurs within 1 day of the 26^{th} day of the cycle
  - If the cycle takes 21 days, ovulation usually occurs within 1 day of the 7^{th} day of the cycle
- Therefore, 4 days before and 3 days after the calculated day of ovulation, intercourse should be avoided

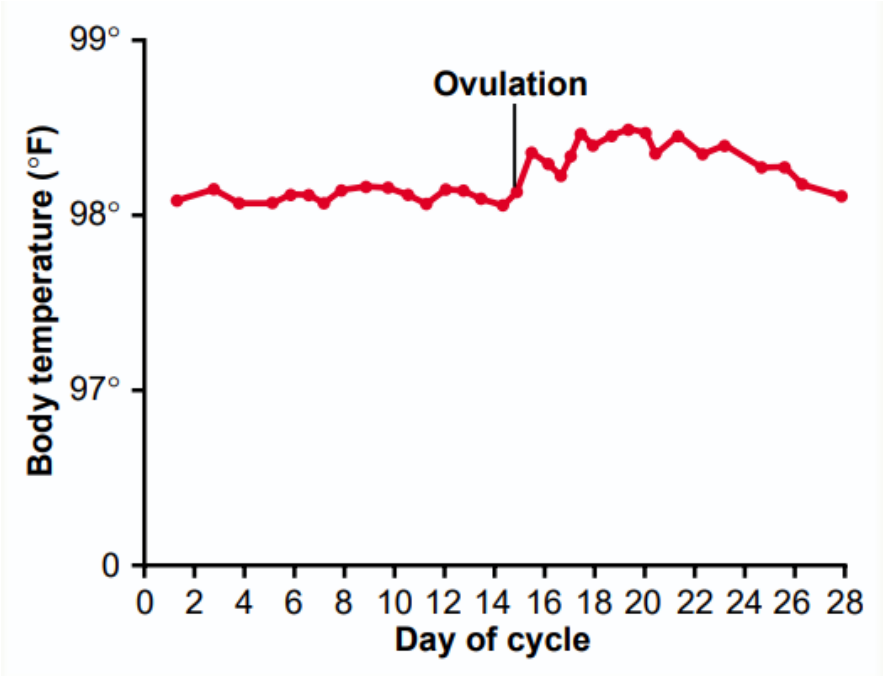
Female Fertility

- **Hormonal Suppression of Fertility—"The Pill."**
- Appropriate administration of either estrogen or progesterone can prevent the preovulatory surge of LH secretion by the pituitary gland, which is essential in causing ovulation
  - The mechanism is not fully understood
- Appropriate combination of estrogens and progestins is essential for avoiding unwanted effects such as abnormal menstrual bleeding patterns
  - Almost all "pills" used for the control of fertility consist of some combination of synthetic estrogens and synthetic progestins
  - The main reason for using synthetic estrogens and progestins is that the natural hormones are almost entirely destroyed by the liver within a short time after they are absorbed from the gastrointestinal tract into the portal circulation but the synthetic hormones can resist this destruction and can be used orally

Contraceptive Pills

Abnormal Conditions That Cause Female Sterility

- About 5 to 10 per cent of women are infertile
- Failure to ovulate
  - By far, the most common cause of female sterility is failure to ovulate
  - hyposecretion of gonadotropic hormones
  - abnormal ovaries that do not allow ovulation
- Diagnosis (Dx): based on progesterone secretion
  1. During the 2nd half of the sexual cycle, progesterone is given and then surge of pregnanediol, the end product of progesterone in urine would be measured.
     - the lack of this substance indicates failure of ovulation
  2. Chart the woman's body temperature throughout the cycle. Secretion of progesterone during the 2nd half of the cycle raises the body temperature about 0.5°F (0.3°C), with the temperature rise coming abruptly at the time of ovulation



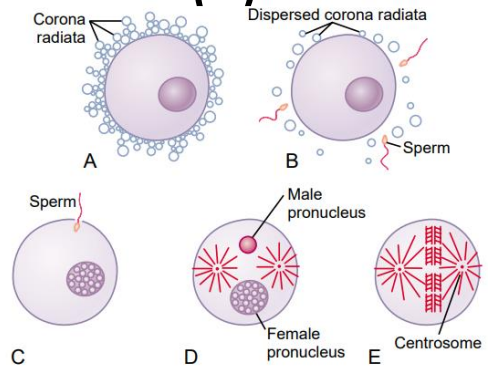
Abnormal Conditions That Cause Female Sterility

- **Treatment (Tx):**
  - Appropriately timed administration of human chorionic gonadotropin (hCG), a hormone that is extracted from the human placenta
  - It has almost the same effects as LH and is therefore a powerful stimulator of ovulation
  - Excess use of this hormone can cause superovulation which results in multiple births
- **Endometriosis:**
  - Is one of the most common causes of female sterility
  - Uterine endometrium grows and even menstruates in the pelvic cavity surrounding the uterus, fallopian tubes, and ovaries
  - It causes fibrosis throughout the pelvis, and sometimes ovaries cannot release the ovum
- **Salpingitis:**
  - Inflammation of the fallopian tubes (not so common)
  - Causes fibrosis in the tubes, thereby occluding them
  - In the past, such inflammation occurred mainly as a result of gonococcal infection
- **Secretion of abnormal mucus by the uterine cervix:**
  - Infection, inflammation, or abnormal hormonal stimulation of the cervix can lead to a viscous mucous plug that prevents fertilization

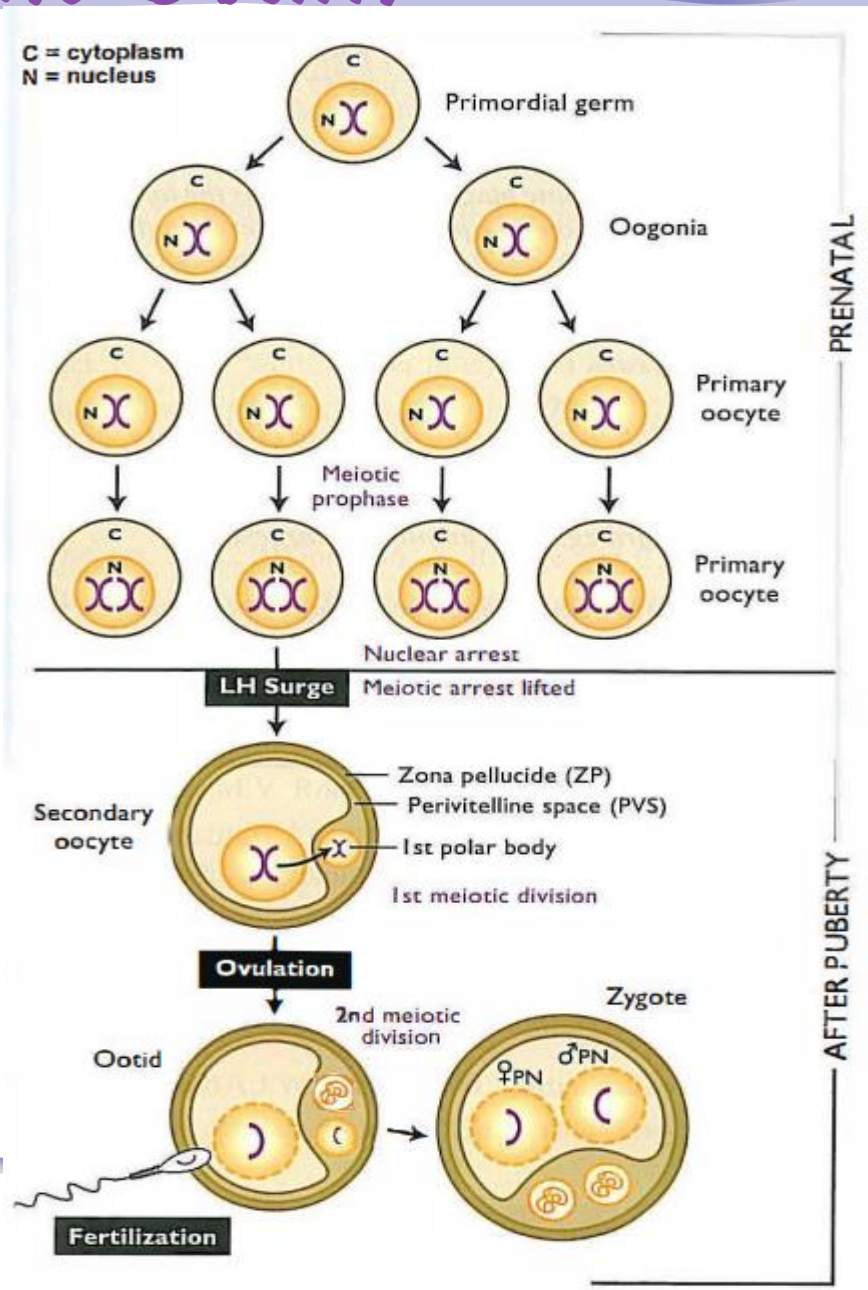
Pregnancy

Maturation and Fertilization of the Ovum

- **Before puberty:**
  - The ovum in the ovary is called: primary oocyte (2n)
  - Meiosis-I starts and arrests at prophase-1
- **After puberty:**
  - Shortly before ovulation meiosis-1 completes
    → secondary oocyte (n) and first polar body
  - Meiosis-2 begins and arrest at metaphase-2 → Ovulation
  - If fertilization occurs, meiosis-2 completes
    → female pronucleus (n) and second polar body forms
    → Zygote

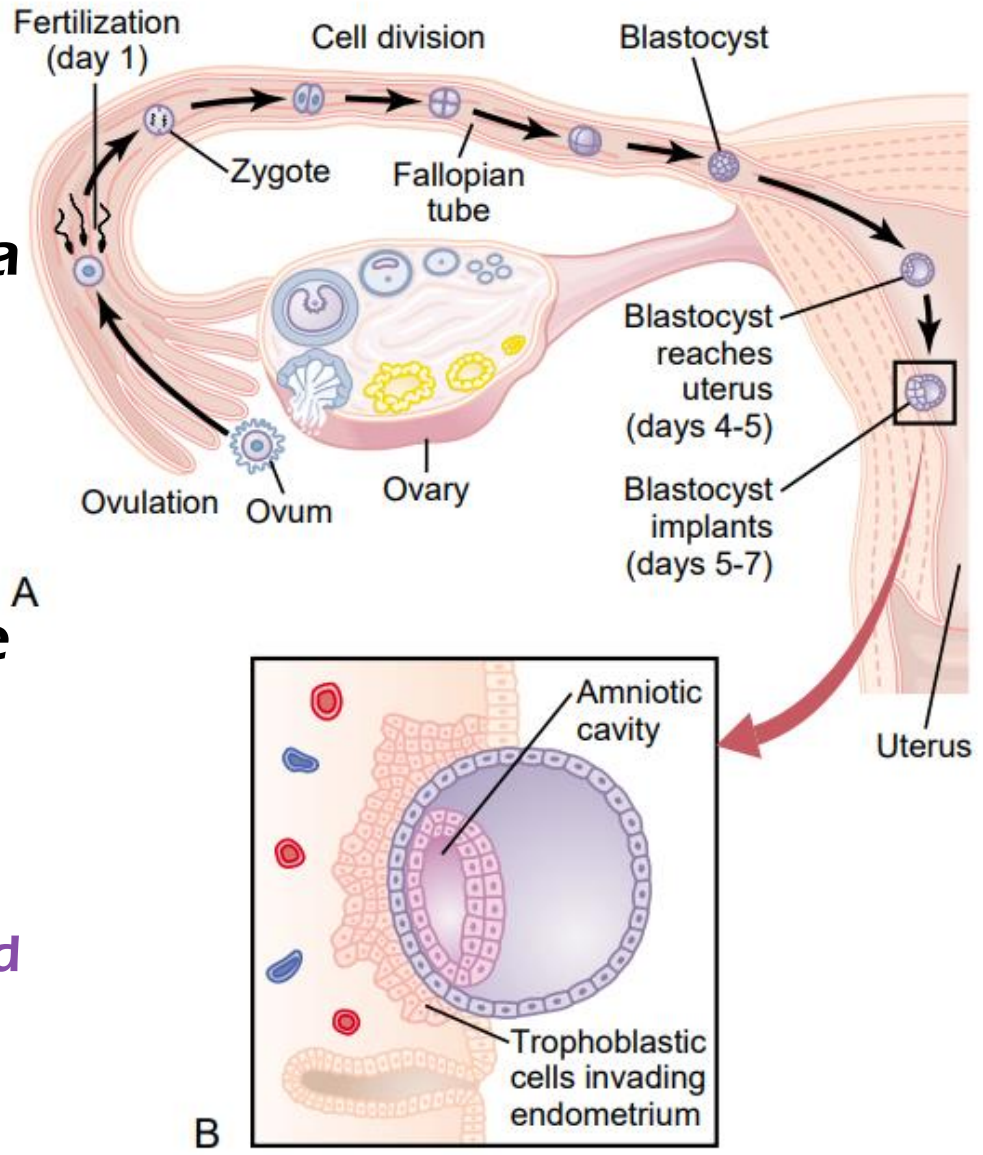


- If fertilization does not occur, secondary oocyte destroys



Maturation and Fertilization of the Ovum

- When ovulation occurs, the ovum, expels directly into the peritoneal cavity and must then enter one of the fallopian tubes
- After the male ejaculates semen into the vagina during intercourse, a few sperm are transported within 5 to 10 minutes upward from the vagina and through the uterus and fallopian tubes to the ampullae of the fallopian tubes near the ovarian ends of the tubes where fertilization occurs
- Transport of the sperm is aided by:
  - contractions of the uterus and fallopian tubes stimulated by prostaglandins in the male seminal fluid
  - oxytocin released from the posterior pituitary gland of the female during her orgasm

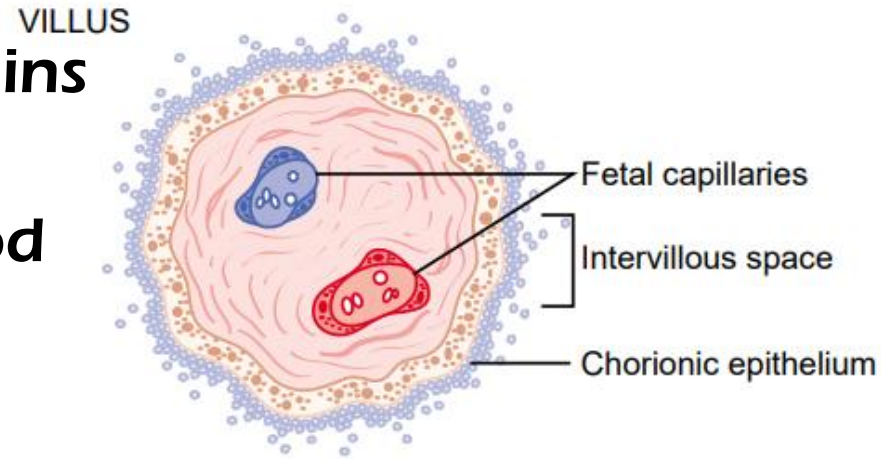


Oogenesis, Graafian Follicle and Corpus Luteum

Fertilization and Implantation

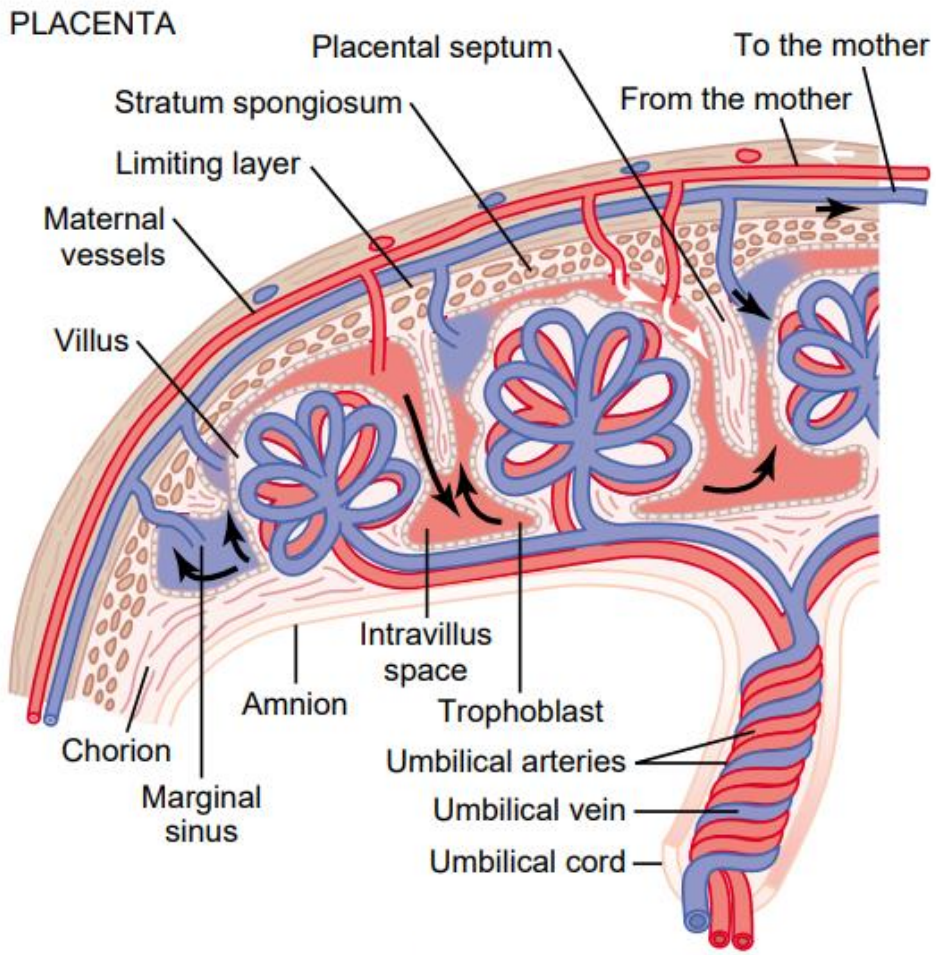
Function of the Placenta

- While the trophoblastic cords from the blastocyst are attaching to the uterus, blood capillaries grow into the cords from the vascular system of the newly forming embryo
- By the 16th day after fertilization, blood also begins to be pumped by the heart of the embryo itself
- Simultaneously, blood sinuses supplied with blood from the mother develop around the outsides of the trophoblastic cords
- The trophoblast cells send out more and more projections, which become placental villi into which fetal capillaries grow
- Thus, the villi, carrying fetal blood, are surrounded by sinuses that contain maternal blood



Function of the Placenta

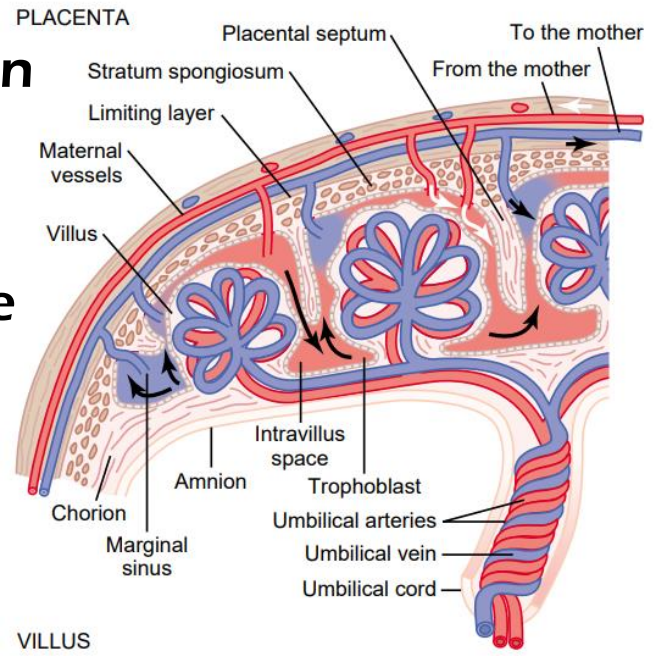
- The fetus's blood flows through two umbilical arteries, then into the capillaries of the villi, and finally back through a single umbilical vein into the fetus.
- The mother's blood flows from her uterine arteries into large maternal sinuses that surround the villi and then back into the uterine veins of the mother
- Nutrients and other substances pass through the placental membrane mainly by diffusion



Function of the Placenta

Diffusion of O_2 Through the Placental Membrane

- The dissolved oxygen in the blood of the large maternal sinuses passes into the fetal blood by simple diffusion, driven by an oxygen pressure gradient from the mother's blood to the fetus's blood



Diffusion of CO_2 Through the Placental Membrane

- The PCO_2 of the fetal blood is 2 to 3mm Hg higher than that of the maternal blood
- Because of extreme solubility, CO_2 easily diffuses through placental membrane even with this small pressure gradient

Diffusion of Foodstuffs Through the Placental Membrane

- Glucose: Facilitated diffusion, Fatty Acids: Diffusion (but more slowly than glucose), Electrolytes: Diffusion (relatively easy)

Excretion of Waste Products Through the P.M.

- Nonprotein nitrogens such as urea, uric acid, and creatinine mainly diffuse across the placental membrane as a result of diffusion gradient

Understanding the Placenta

Hormonal Factors in Pregnancy

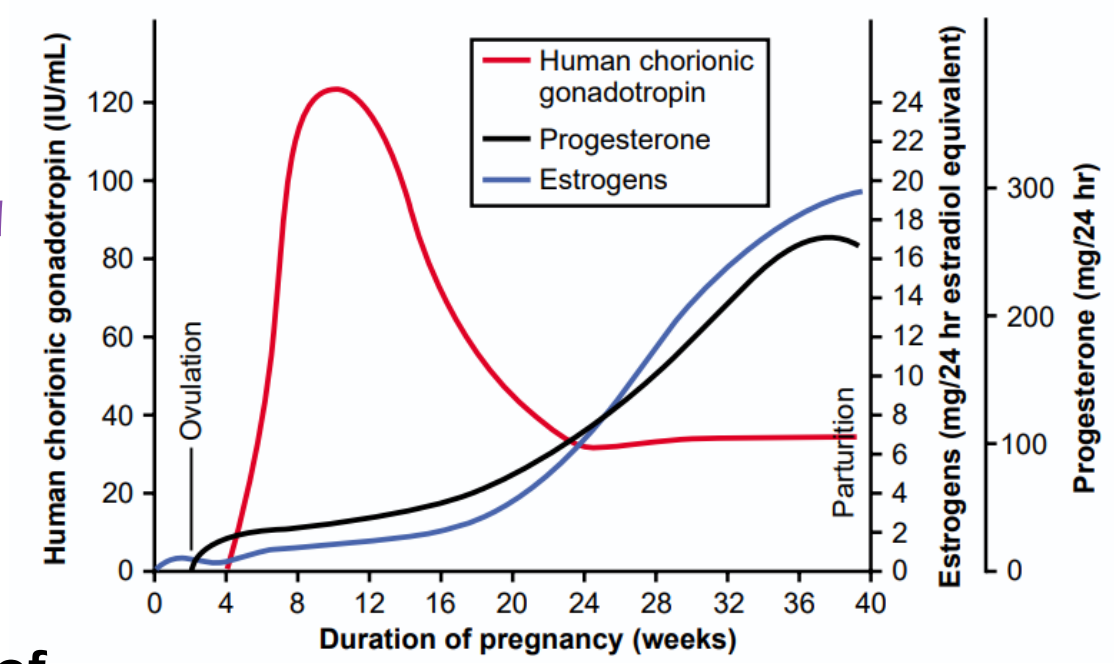
- In pregnancy, the placenta forms especially large quantities of human chorionic gonadotropin (hCG), estrogens, progesterone, and human chorionic somatomammotropin,
  - The first three of which, and probably the fourth as well, are all essential to a normal pregnancy

- Almost all the nonsexual endocrine glands of the mother also react markedly to pregnancy
  - This results mainly from the increased metabolic load on the mother
  - The effects of placental hormones on the mother's pituitary and other glands

Effects of Placental hCG on Pregnancy

- "hCG" is secreted by the syncytial trophoblast cells into the fluids of the mother
  - Can first be measured in the blood 8 to 9 days after ovulation, shortly after the blastocyst implants in the endometrium (Baby check rapid tests measures this hormone in the urine)

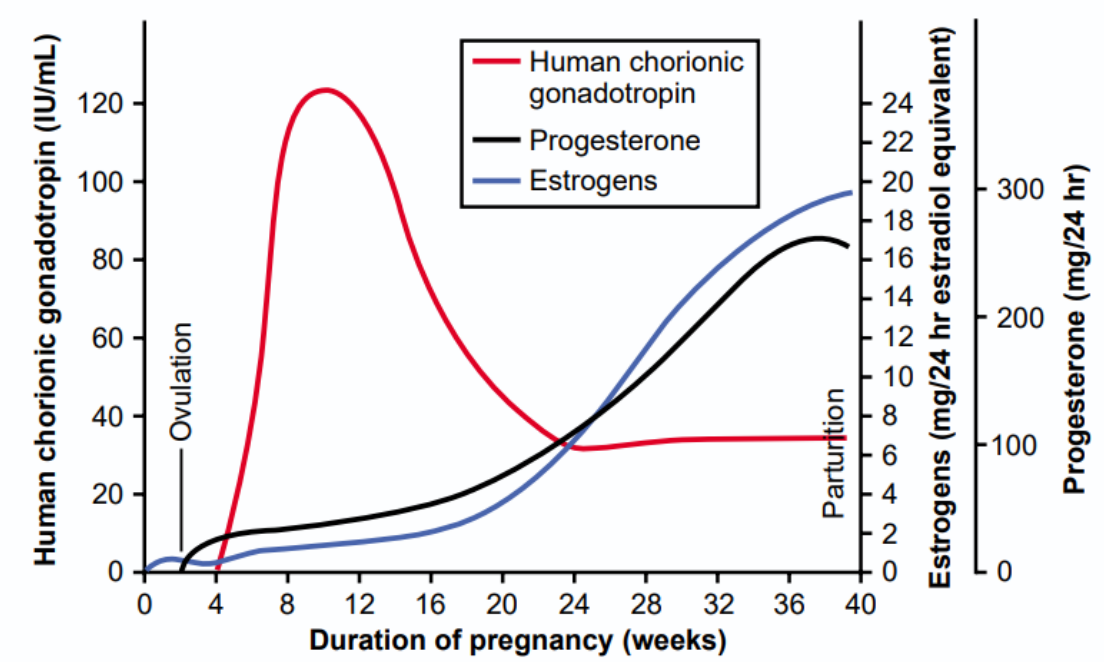
- "hCG" function:
  - Prevent involution of the CL at the end of the monthly cycle
  - Causes the CL to secrete even larger quantities of progesterone and estrogens
  - prevent menstruation
  - cause the endometrium to continue to grow



Effects of Placental hCG on Pregnancy

- If the CL is removed before approximately the 7th to 12th week of pregnancy, spontaneous abortion almost always occurs
  - After that time, the placenta secretes sufficient quantities of progesterone and estrogens to maintain pregnancy

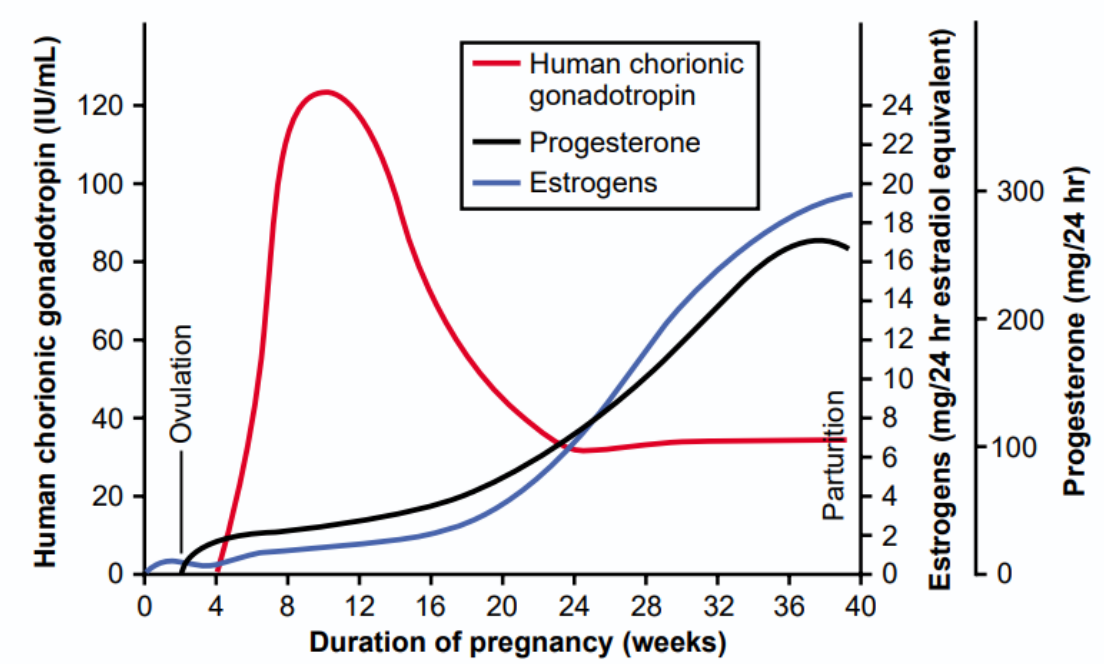
- "hCG" has an interstitial cell–stimulating effect on the testes of the male fetus, resulting in production of testosterone
  - Causes the grow of male sex organs
  - Descending testes into the scrotum



Effects of Placental Estrogens on Pregnancy

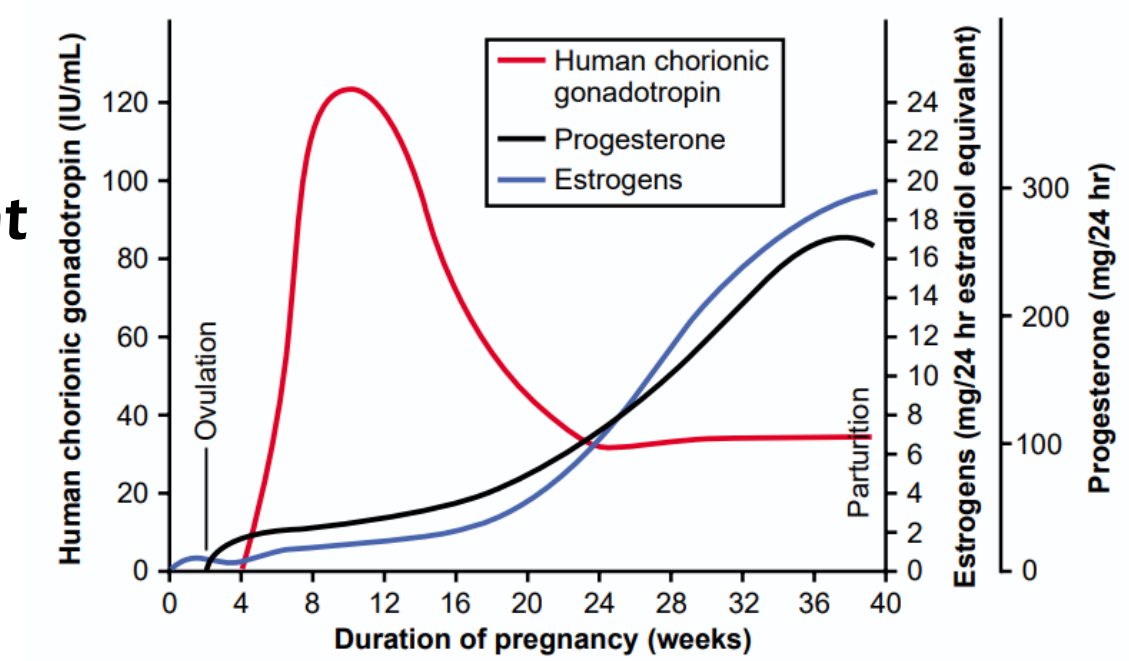
- The estrogens mainly have a proliferative function on most reproductive and associated organs of the mother

- During pregnancy, the extreme quantities of estrogens cause
  - Enlargement of the mother's uterus
  - Enlargement of the mother's breasts and growth of the breast ductal structure
  - Enlargement of the mother's female external genitalia



Effects of Placental Progesterone on Pregnancy

- Causes decidual cells to develop in the uterine endometrium to feed the early embryo
- Decreases the contractility of the pregnant uterus to prevent spontaneous abortion
- Contributes to the development of the conceptus even before implantation by providing appropriate nutritive matter for the developing morula and blastocyst
- Helps the estrogen prepare the mother's breasts for lactation



Human Chorionic Somatomammotropin

- Causes at least partial development of the animal's breasts and in some instances causes lactation (Human placental lactogen)
- Has weak actions similar to those of growth hormone
- Causes decreased insulin sensitivity and decreased utilization of glucose in the mother, thereby making larger quantities of glucose available to the fetus
- Further, the hormone promotes the release of free fatty acids from the fat stores of the mother, thus providing this alternative source of energy for the mother's metabolism during pregnancy

Other Hormonal Factors in Pregnancy

- Secretion of the glucocorticoids from adrenal cortex moderately increases
  - Help mobilize amino acids from the mother's tissues so that these can be used for synthesis of tissues in the fetus
- Aldosterone secretion increase about two folds
  - Reabsorb excess sodium from the mother's renal tubules and, therefore, to retain fluid, occasionally leading to pregnancy-induced hypertension
- The mother's thyroid gland ordinarily enlarges up to 50 per cent during pregnancy and increases its production of thyroxine a corresponding amount
- The mother's parathyroid glands usually enlarge during pregnancy
  - Causes calcium absorption from the mother's bones, thereby maintaining normal Ca^{++} concentration in the mother's ECF
  - This secretion of PTH is even more intensified during lactation after the baby's birth because the growing baby requires many times more Ca^{++} than the fetus does
- Relaxin softens the cervix of the pregnant woman at the time of delivery

Response of the Mother's Body to Pregnancy

- The most apparent reaction of the mother to the fetus is the increased size of the various sexual organs such as uterus, vagina and breasts.
  - Various hormones can cause marked changes in a pregnant woman's appearance, like edema, acne, and masculine or acromegalic features

Weight Gain in the Pregnant Woman

- The average weight gain during pregnancy is about 11kg, with most of this gain occurring during the last two trimesters.
  - Of this, about 3kg is fetus and the rest is amniotic fluid, placenta, uterus, breasts, blood and extracellular fluid and fat accumulation
  - Increased appetite: 1) fetus feeding, 2) hormonal factors

If not controlled properly: weight gain would reach up to 34kg!

Response of the Mother's Body to Pregnancy

Metabolism During Pregnancy

- The basal metabolic rate increases about 15 per cent during the 2nd half of pregnancy due to the increased secretion of thyroxin, adrenocortical and sex hormones
  - She frequently feels overheated
  - Needs more energy for muscle activity due to the extra load that she is carrying

Nutrition During Pregnancy

- If appropriate nutritional elements are not present in a pregnant woman's diet, a number of maternal deficiencies can occur, especially in calcium, phosphates, iron, and the vitamins
  - Multivitamin supplements especially for vitamin D, E and K as well as iron should be use by pregnant women

Response of the Mother's Body to Pregnancy

Maternal Body System Changes During Pregnancy

- In the 27th week of pregnancy, the mother's cardiac output is 30 to 40 per cent above normal but during the last 8 weeks of pregnancy it gets back nearly to normal
- The maternal blood volume shortly before term is about 30 per cent above normal
  - Increased aldosterone and estrogens
  - Increased fluid retention by the kidneys
- Respiratory rate (minute ventilation) increases about 50% during pregnancy
  - Increased basal metabolic rate
  - High levels of progesterone increases the respiratory center's sensitivity to carbon dioxide
  - The growing uterus presses upward against the abdominal contents, and these press upward against the diaphragm

Response of the Mother's Body to Pregnancy

Maternal Body System Changes During Pregnancy

- the normal pregnant woman ordinarily accumulates only about 6 pounds (~3Kg) of extra water and salt
  - Increased reabsorptive capacity for sodium, chloride, and water
  - Increased the glomerular filtration rate (GFR) as much as 50 per cent

- The water in amniotic fluid is replaced once every 3 hours, and the electrolytes sodium and potassium are replaced an average of once every 15 hours

Preeclampsia and Eclampsia

- Rapid rise in arterial blood pressure to hypertensive levels during the last few months of pregnancy and severe proteinuria is called preeclampsia or toxemia of pregnancy
  - Excess salt and water retention by the mother's kidneys, weight gain, edema and hypertension
  - Impaired function of the vascular endothelium most significantly in the kidneys, brain, and liver
  - RBF and GFR decrease which is exactly opposite to the changes that occur in the normal pregnant woman
  - Three possible explanations:
    - Excessive secretion of placental or adrenal hormones
    - Some type of autoimmunity or allergy in the mother caused by the presence of the fetus
    - Insufficient blood supply to the placenta, resulting the release of TNF-a and IL-6
- Eclampsia is an extreme degree of preeclampsia, characterized by vascular spasm throughout the body; clonic seizures in the mother, sometimes followed by coma and death
  - With using vasodilating drugs and immediate termination of pregnancy it can be cured

Parturition

Increased Uterine Excitability Near Term

- Toward the end of pregnancy, the uterus becomes progressively more excitable, until finally it develops such strong rhythmical contractions that the baby is expelled

Hormonal Factors That Increase Uterine Contractility

- Increased Ratio of Estrogens to Progesterone
- Secretion of Oxytocin by mother's pituitary
- Secretion of Oxytocin, Cortisol and prostaglandins by the fetus

Mechanical Factors That Increase Uterine Contractility

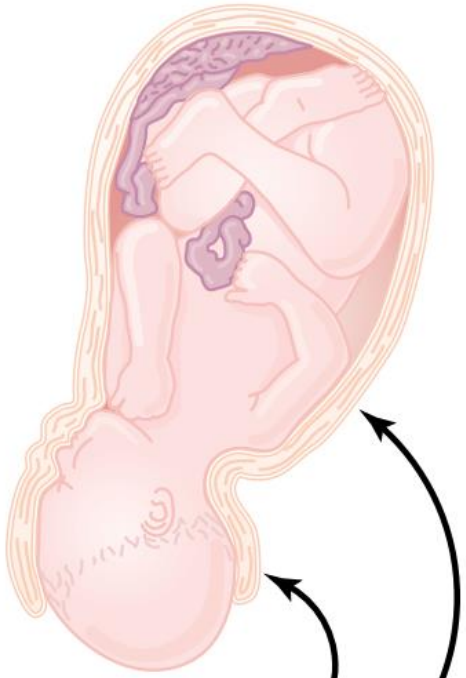
- Stretch of the Uterine Musculature
- Stretch or Irritation of the Cervix

Onset of Labor

- Braxton Hicks contractions: weak and slow rhythmical contractions during pregnancy
- Labor contractions: exceptionally strong contractions that start stretching the cervix and later force the baby through the birth canal

Positive Feedback Mechanism

- The positive feedback theory suggests that stretching of the cervix by the fetus's head finally becomes great enough to elicit a strong reflex increase in contractility of the uterine body
- Cervical stretching also causes the pituitary gland to secrete oxytocin, which is another means for increasing uterine contractility



1. Baby's head stretches cervix
2. Cervical stretch excites fundic contraction
3. Fundic contraction pushes baby down and stretches cervix some more
4. Cycle repeats over and over again

Abdominal Muscle Contractions During Labor

- The uterine contractions during labor begin mainly at the top of the uterine fundus and spread downward
- The intensity of contraction is great in the top and body of the uterus but weak in the lower segment of the uterus adjacent to the cervix, to force the baby downward toward the cervix
  - In the early part of labors: once every 30 minutes
  - The combined contractions of the uterine and abdominal musculature during delivery of the baby cause a downward force on the fetus toward the birth canal
- Contractions of labor occur intermittently, because strong contractions impede or sometimes even stop blood flow through the placenta and would cause death of the fetus
  - Overuse of various uterine stimulants, such as oxytocin, can cause uterine spasm rather than rhythmical contractions and can lead to death of the fetus

Abdominal Muscle Contractions During Labor

- The first stage of labor is a period of progressive cervical dilation, lasting until the cervical opening is as large as the head of the fetus
  - Usually lasts for 8 to 24 hours in the first pregnancy but often only a few minutes after many pregnancies
- The second stage of labor is characterized by fetal membrane rupture and flowing of amniotic fluid through vagina
  - It may last from as little as 1 minute after many pregnancies to 30 minutes or more in the first pregnancy
- The third stage of labor is separation and delivery of the placenta
  - For 10 to 45 minutes after birth of the baby, the uterus continues to contract to a smaller and smaller size, which causes a shearing effect between the walls of the uterus and the placenta, thus separating the placenta from its implantation site

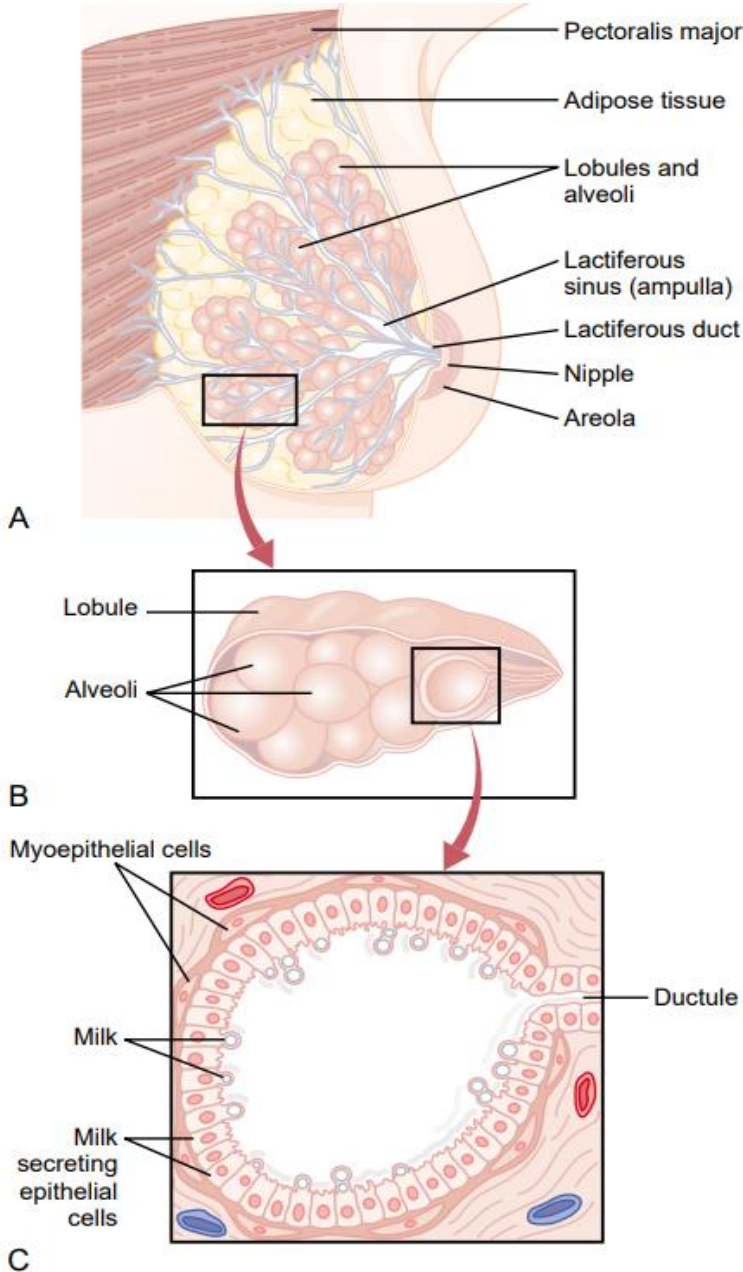
Involution of the Uterus After Parturition

- During the first 4 to 5 weeks after parturition, the uterus involutes
  - Its weight becomes less than half within 1 week.
  - In 4 weeks, if the mother lactates, the uterus may become as small as it was before pregnancy because of the suppression of pituitary gonadotropin and ovarian hormone secretion during the first few months of lactation
- During early involution of the uterus, the placental site on the endometrial surface autolyzes, causing a vaginal discharge known as "lochia," which is first bloody and then serous in nature, continuing for a total of about 10 days

Lactation

Development of the Breasts

- The breasts begin to develop at puberty stimulated by the estrogens of the monthly female sexual cycle
- All through pregnancy, the large quantities of estrogens secreted by the placenta cause the ductal system of the breasts to grow and branch
- at least four other hormones are also important for growth of the ductal system:
  - Growth hormone, Prolactin, the Adrenal glucocorticoids, and Insulin
- Once the ductal system has developed, progesterone—acting synergistically with estrogen, as well as with the other hormones just mentioned—causes additional growth of the breast lobules, with budding of alveoli and development of secretory characteristics in the cells of the alveoli

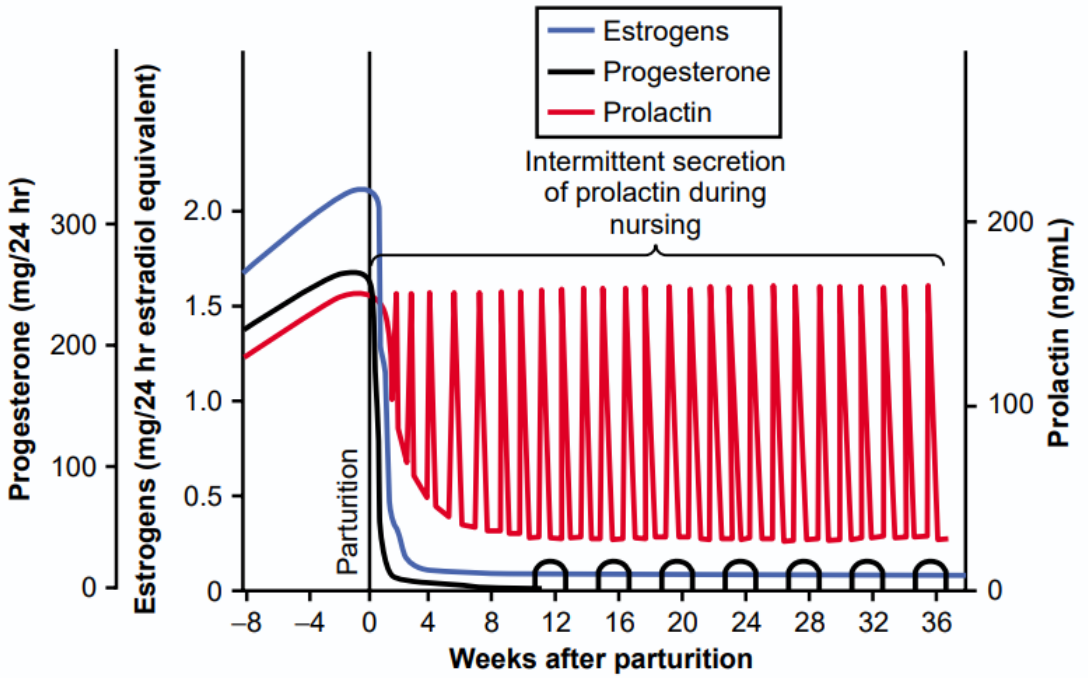


Initiation of Lactation

- Estrogen and progesterone inhibit the actual secretion of milk
- Conversely, the hormone prolactin promotes the milk secretion
- Prolactin concentration in mother's blood rises steadily from the fifth week of pregnancy until birth of the baby, 10 to 20 times more than the normal nonpregnant level
- The placenta secretes large quantities of human chorionic somatomammotropin, which probably has lactogenic properties
- The fluid secreted during the last few days before and the first few days after parturition is called colostrum
  - The same concentrations of proteins and lactose as milk
  - Almost no fat
  - Production rate is about 1/100 of subsequent rate

Initiation of Lactation

- Immediately after birth, estrogen and progesterone secretion drops and prolactin rise to produce milk
  - adequate background secretion of the mother's growth hormone, cortisol, parathyroid hormone, and insulin is needed for this process
- After birth of the baby, the basal level of prolactin secretion returns to the nonpregnant level over the next few weeks
  - However, each time the mother nurses her baby, nervous signals from the nipples to the hypothalamus cause a 10- to 20-fold surge in prolactin secretion that lasts for about 1 hour
  - If this prolactin surge is absent or blocked as a result of hypothalamic or pituitary damage or if nursing does not continue, the breasts lose their ability to produce milk within 1 week or so



Ejection (or "Let-Down") Process in Milk Secretion

- When the baby suckles, it receives virtually no milk for the first half minute or so
- Sensory impulses must first be transmitted to hypothalamus, where they cause nerve signals that promote oxytocin secretion at the same time that they cause prolactin secretion
- The oxytocin causes myoepithelial cells to contract, thereby expressing the milk from the alveoli into the ducts at a pressure of +10 to 20 mm Hg
  - Thus, within 30 seconds to 1 minute after a baby begins to suckle, milk begins to flow. This process is called milk ejection or milk let-down
- Suckling on one breast causes milk flow not only in that breast but also in the opposite breast
- It is especially interesting that fondling of the baby by the mother or hearing the baby crying often gives enough of an emotional signal to the hypothalamus to cause milk ejection

Good Luck !