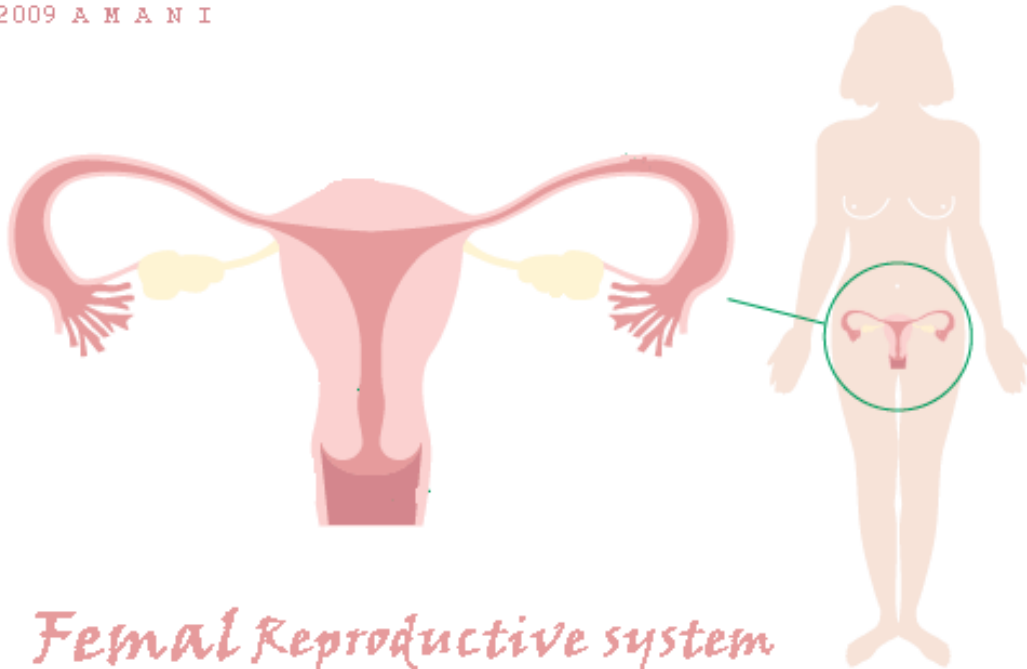


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*Female Reproductive system*

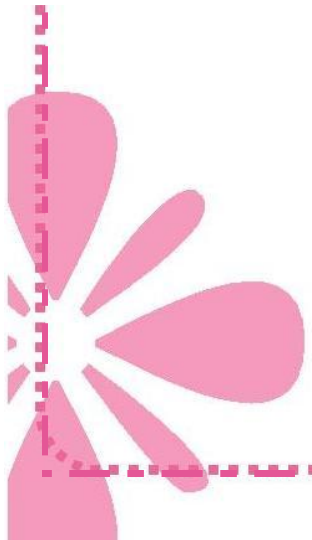
**Done By**

*Amani AlBijadi*

**Special thanks to**

Mona AlFara'ady

Gadeer radwan



## FEMALE SEXUAL SYSTEM (MENSTRUAL CYCLE)

The reproductive years of a female are characterized by mostly rhythmic changes in the rate of secretion of *female hormones* and corresponding changes *in ovaries and sexual organs*. The duration of each cycle averages **28 days** (20-45)

The cycle is initiated by age **11-13 years** when the *hypothalamus* release **LHRH** at age of **9-10 years**. This stimulates *AP gland* to secrete **FSH** and **LH** which are essential for full secretion of ovaries. The period of change is called *puberty*.

**PUBERTY:** period of change.

**MENARCHE:** first cycle.

### Significance of Female Sexual Cycle

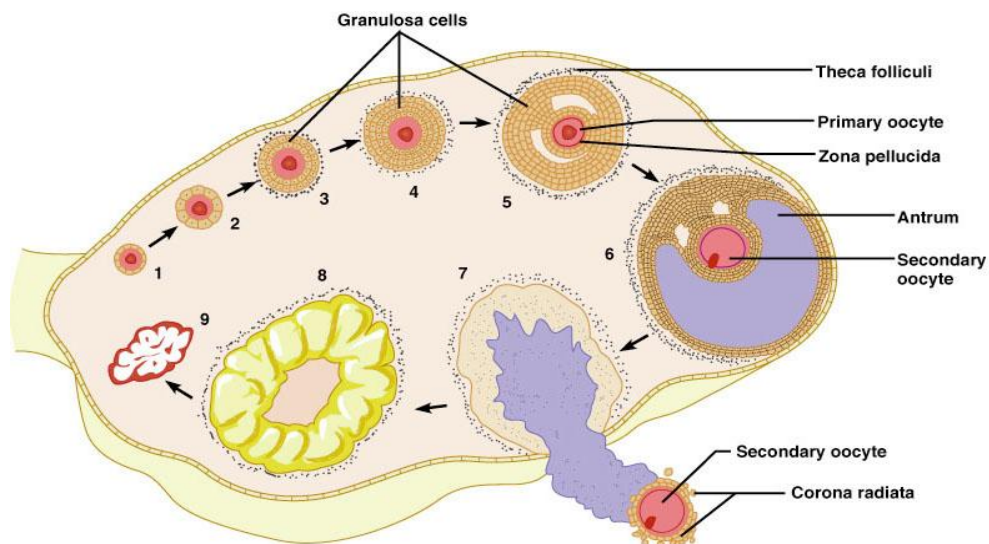
- 1- Release of single mature ovum from the ovaries each month.
- 2- Preparation of uterine endometrium for implantation of fertilized ovum.

### Ovarian Cycle

**Changes in ovaries during each cycle can be divided into:**

- 1- Follicular phase.
- 2- Ovulatory process.
- 3- Luteal phase.

### Follicular Phase



- **Ovaries contain many primordial follicles.** Each of these immature follicles is formed of ova called **primary oocyte** surrounded by single layer of granulosa cells and theca cell layer. **primary oocytes** decrease in number throughout a women's life. The ovaries of a newborn girl contain about 2 millions oocytes.

- **By puberty, the number of oocytes and follicles has been reduced by 400,000.** Only about 400 of these oocytes ovulate during reproductive years and the rest will die by **apoptosis**. Oocytes cease entirely by **menopause**.
- **Under the influence of FSH and LH, the ovaries and follicles will to grow.** Granulosa cells proliferate into several layers with fluid spaces and begin to synthesize estrogen in response to **FSH**.
- **The oocytes now secondary oocytes enlarge and become surrounded by a layer of granulosa cells corona radiata,** another layer of granulosa cells *cumulus oophorus* and zona pellucida mucopolysaccharide layer. It represents a barrier to the sperm to fertilize an ovulated ovum.
- **As follicles develop, primary oocyte completes its first meiotic division.** This does not form 2 complete cells because only one cell secondary oocyte gets all the cytoplasm. The other cell formed at this time becomes a small polar body which usually disappears. The secondary oocyte then begins the second meiotic division which is completed when the ovum is fertilized.
- **During meiosis each primary oocyte produces single haploid gamete.** If secondary oocyte is fertilized, it forms a secondary polar body and becomes a zygote.
- **Theca cells differentiate into 2 layers and respond to LH** by synthesizing androgens which transform into progesterone by granulosa cells.
- **The rising levels of estrogen exert negative feedback effect on FSH secretion causing it to decline towards mid-cycle.** Estrogen together with increase sensitivity of PG to GnRH cause positive feedback effect on LH and FSH causing peak of LH during mid cycle which leads to LH surge which is essential for ovulation to occur.

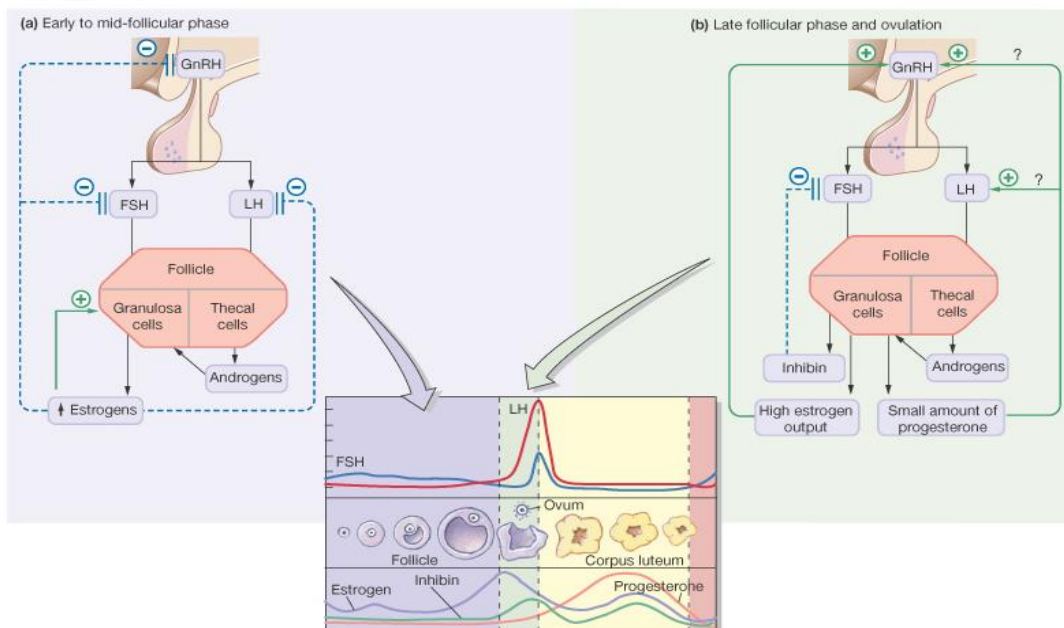
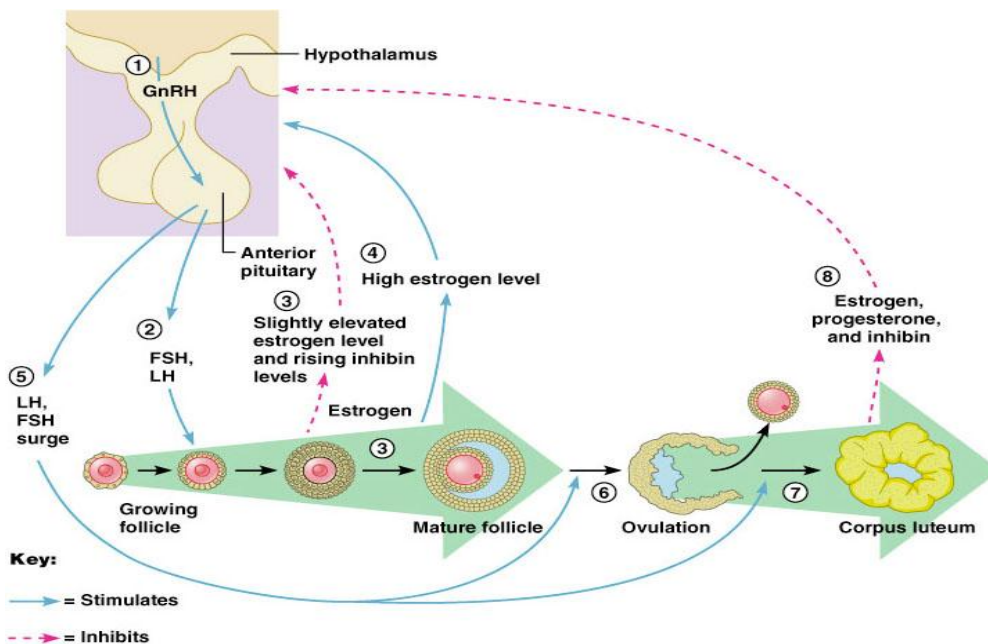
### **Ovulatory Process**

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- Occurs **24-36** hours following **LH** surge (peak) between **12th** and **15th** day of the 28 days menstrual cycle.
- The **LH** surge is produced by a **+ve feedback** effect of **estrogen** secreted in large amounts when one follicle has completed its growth to become a fully mature graffian follicle .The other follicle regress and becomes atretic ( death ), fibrous tissue.
- The ovum swells rapidly. Enzymatic digestion of follicular wall leads to rupture and the ovum is shed. The released cell is *secondary oocyte* . Mid cycle surge of LH terminates the follicular phase and mark the luteal phase.

## Luteal Phase

- **After ovulation**, LH acts on follicular cells which differentiate into luteal cells and corpus luteum (yellow body) is formed (luteinization).
- LH begins to secrete **progesterone** in addition to **estrogen**. Rising levels of these hormones inhibit secretion of **FSH & LH** by **-ve feedback**. There is evidence that corpus luteum produces **inhibin** which suppress LH secretion or action.
- Loss of those 2 hormones causes corpus luteum to degenerate (if no pregnancy takes place) and is replaced by CT and becomes corpus albicans. Degeneration of corpus luteum causes **estrogen & progesterone** levels to decrease and remove the **-ve feedback** effect from PG allowing rise of FSH to stimulate maturation of more follicles for next cycle.



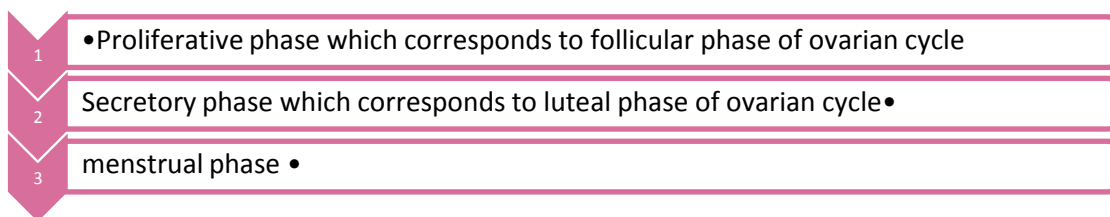
## Uterine (endometrial) cycle

Myometrium and endometrium undergo important changes in response to estrogen and progesterone (*changes corresponding to ovarian changes*)

### Myometrial changes

Estrogen increases uterine blood flow & myometrial activity while progesterone decreases myometrial activity (smooth muscle less active, relaxed) to prevent abortion. This is important to ensure minimal uterine activity in case of early implantation.

### Endometrial changes



#### 1-Proliferative phase

Estrogen is responsible for this phase. It occurs when the ovary is in the follicular phase and lasts from end of menstruation till end of ovulation. After menstruation, a thin layer of endometrial stroma remains.

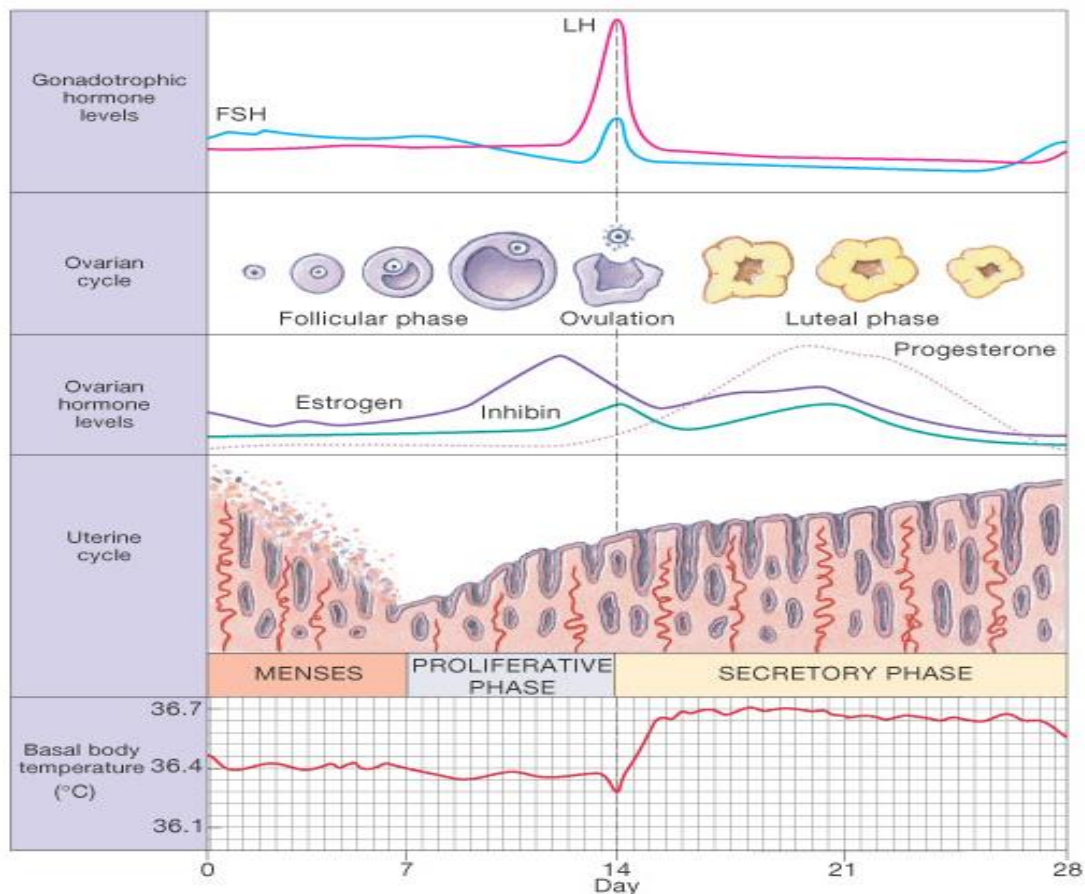
Under the influence of estrogen, stromal cells proliferate, endometrial glands become long and tortuous. Blood supply of endometrium grows and become coiled and is called spiral arteries.

During this period, endometrium grows from 0.5-5 mm in height. Estrogen also stimulates the production of receptor proteins for progesterone, in preparation for the next phase of cycle.

#### 2-Secretory Phase

It occurs when the ovary is in the luteal phase and lasts from ovulation till menstruation. Progesterone is the dominant hormone.

Estrogen causes slight additional cell proliferation in endometrium. Progesterone causes functional changes in endometrium to prepare it for implantation. The glands increase in tortuosity and acquire secretory activity. The arteries become prominent and coiled.



*Further changes depend on whether implantation has taken place or not.*

**1\ Implantation :** If pregnancy takes place, embryo secretes HCG from placenta that maintains corpus luteum, so the secretion of estrogen and progesterone is maintained. Stromal cells proliferate and differentiate into layers.

### **2\ Non Implantation**

No HCG, Corpus luteum declines, estrogen and progesterone levels decrease. This results in reduction of in endometrial tissue weight and more coiling of arteries with secondary ischemia and blanching of endometrium.

### **Menstruation**

- 1) It occurs as a result of the **fall** of ovarian **estrogen and progesterone** during luteal phase due to degeneration of corpus luteum. Interstitial hemorrhage occurs as a result of breakdown of superficial arteries and capillaries. The superficial endometrial layers are shed, necrotic tissues are extruded into uterine cavity and initiate uterine contractions to expel contents.
- 2) **Volume** is **50-70 mls** which is mostly arterial blood with only 25% of it venous blood. It contains tissue debris, prostaglandins, fibrinolysin (*to prevent blood clotting, mucous membranes contain no clots*), and large number of leukocytes for defense against infections. The menstrual flow stops in 5-7 days.
- 3) Resumption of estrogen secretion by the newly developing follicles reduces bleeding and new tissue growth.



## Abnormalities of menstrual cycle :

- **Amenorrhea:**

**-primary Amenorrhea:** Failure to menstruate at puberty

**-secondary Amenorrhea:** Cessation of the normal cycle as with pregnancy

- **Dysmenorrhea:** Occurrence of pain during menstruation (normally occurs)
- **Oligomenorrhea:** Little blood flow during menstruation
- **Menorrhagia:** Excessive bleeding during menstruation (with blood clots)
- **Metrorrhagia:** Abnormal uterine bleeding which is not associated with menstruation and occurs at irregular intervals often due to ovarian or uterine diseases.

### *Changes in Cervix during Uterine Cycle*

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During the proliferative phase, cervical mucus is thin and alkaline. After ovulation, mucus becomes thick and difficult to penetrate in order to protect the uterus and prevent excess entry of sperms.

### *Changes in Vagina during Uterine cycle*

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During the proliferative phase, estrogens cause vaginal epithelium to be cornified. After ovulation, progesterone increases vaginal secretion.

### *Anovulatory Cycle*

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Ovulation does not always occur during the first cycle following puberty and prior to menopause, when LH surge is not potent to cause ovulation.

Lack of ovulation causes failure of development of the corpus luteum and no secretion of progesterone during the second half of the cycle. The cycle is shortened but the rhythm continues (*every 20-18 days, but menstruation still occurs*)

### *Signs of Ovulation*

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- 1- Detection of secretory phase in an endometrial biopsy.
- 2- Rise of body temperature, by 0.3-0.5 degree at mid cycle with lower abdominal pain
- 3- Thick cervical mucus during the second half of the cycle, while in the first half it is thin.
- 4- Rise of blood progesterone level and its urinary output.

# Ovarian Hormones

## Estrogens

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- Main natural estrogen is  $17\beta$  estradiol, estrone, and estriol( differ in activity) . $17\beta$  estradiol is most active, while estriol is the least.

### Secreted by:

- 1- Granulosa cells of ovarian follicles
  - 2- Corpus luteum during second half of the cycle
  - 3- Placenta during pregnancy
  - 4- Adrenal cortex
- 97% of estradiol is bound to plasma proteins
  - Estrogens are metabolized in the liver and excreted in bile.
  - Secretion occurs in 2 peaks. One peak occurs just **before ovulation** and the other during **mid luteal phase**.
  - After menopause, estrogens decrease to low levels.

### Action of Estrogen (causes proliferation of non-secretory cells)

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- **At PUBERTY**
  - 1- Cellular growth of tissues of sex organs ( external and internal), changing from a child to an adult.
  - 2- Development of secondary sexual characteristics;
    - Development of breast duct system and fat deposition( smooth appearance)
    - Deposition of fat in certain parts; characteristics rounded female figure
    - Growth of axillary and pubic hair with flat topped pattern (androgen effect)
    - Change in body configuration with narrow shoulders and broad hips
    - Voice stays high pitched
    - Skin is soft, smooth, and vascular.
- **Upon reproduction**
  - 1- **Ovaries:** stimulates growth of ovarian follicles
  - 2- **Fallopian tubes:** Increases the motility and activity of ciliated epithelial cells and help fertilization.
  - 3- **Uterus:**
    - Proliferation of endometrium
    - Growth of uterine muscles
    - Increase its content of contractile protein
    - Sensitize uterine muscles to oxytocin
    - Increase uterine blood flow
  - 4- **Breasts; it is the growth hormone of the breast**
    - Increase ductal growth
    - Increase pigmentation of aerola
    - Increase deposition of fat in breast
  - 5- Feedback regulation of gonadotropin secretion
  - 6- Increase libido(sexual desire)
  - 7- Protein anabolic action(+ve nitrogen balance)



- 8- Increase osteoblastic activity and early union of epiphysis
- 9- Salt and water retention by kidney
- 10- Plasma cholesterol lowering effect and decrease incidence of CVS complications
- 11- Large doses increase fibrinogen and promote thrombosis and platelets aggregation
- 12- Secretion of angiotensinogen and TBG (Thyroxin binding globulin) leading to increase in BP
- 13- Increase Formation of adrenal androgens.

### **PROGESTERONE**

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- Produced from corpus luteum by theca lutein cells
- Placenta during pregnancy
- Adrenal cortex
- Bound to plasma proteins
- Metabolized in liver and excreted by kidneys
- Peak progesterone during luteal phase
- **Actions of progesterone :**
  - 1. **Uterus**
    - Secretory changes in mucosal lining of fallopian tubes and in estrogen primed endometrium during luteal phase
    - Antiestrogenic effects on endometrium by decreasing estrogen receptors (no cellular proliferation)
    - Antiestrogenic effect on myometrium making it less excitable and less sensitive to oxytocin
    - During pregnancy, progesterone inhibits uterine activity (relaxing effect), therefore can be used in threatened abortion)
  - 2. **Breast**
    - Increases growth and proliferation of alveolar tissues and lobules to prepare and secrete milk

#### **Other Effect :**

- Thermogenic effect with increase in BMR and body temperature, 24 hours after ovulation
- Stimulation of respiratory center
- Mobilization of protein from mother for fetal use.
- Increase secretion of sebum (sebaceous gland secretion) from skin

### ***Contraceptive Pills (hormonal method of contraception)***

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Administration of synthetic estrogen and progesterone in appropriate quantities during the first half of female cycle can inhibit ovulation by inhibiting LH surge which is essential for ovulation.

Medication is usually began in early stages of monthly cycle and continued beyond time of ovulation (for 3 weeks after the last stage of a menstrual period that is stopped allowing menstruation to occur

There might be an increase risk of breast and cervical cancer from oral contraceptive.

## Menopause

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- Describes the last period or **final cessation of menstruation**
- Occurs in late **40's to early 50's**.
- Women's reproductive abilities decline over **2-3 years** before menopause.
- **Cause of Menopause**; burning out of ovaries at birth. Ovaries contain a certain number of germ cells. As women approach menopause, the ovaries become depleted of oocytes. Ovaries become small and fibrous with no follicles. The circulating estrogen fall to very low levels and cause various effects. When severe those effects are considered abnormal and require treatment. The only estrogen found in blood of menopausal women is the weak estrone formed by cells in adipose tissues. Tissues have higher levels of estrogen and less incidence of osteoporosis.

## Symptoms and signs of menopause

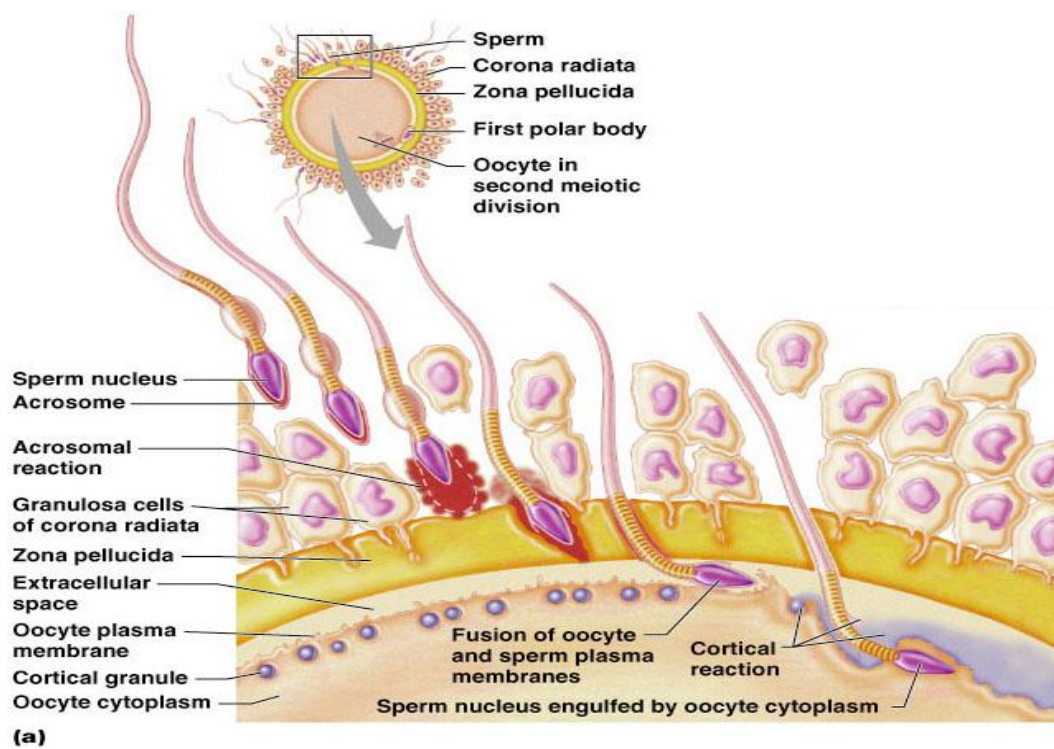
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1. **Vasomotor symptoms** , hot flushes are sensation of warmth on trunk and face with sweating and palpitations
2. **Emotional psychological problems**
3. **Skeletal effects**: increase bone resorption and incidence of fractures. Degenerative changes in joints lead to arthritis. Loss of collagen from skin with loss of elasticity.
4. **CVS problems** as atherosclerotic changes with increase in mortality rate from ischemic heart disease.
5. **Changes in urogenital tract**
  - a. Uterus shrinks and endometrium becomes converted to fibrous tissue. Cervix and vaginal epithelium become atrophic
  - b. External genitalia decrease in size
  - c. Some atrophic changes in urethra

## FERTILIZATION

Shortly before ovum primary oocyte is released from follicle, its nucleus divides by meiosis and a first polar body is expelled primary oocyte becomes secondary oocyte (contains 23 unpaired chromosomes)

When ovulation occurs, secondary oocyte is released and enters the uterine tube. It is surrounded by its zona pelucida and corona radiata of granulosa cells.. Penetration of oocyte by sperm occurs after ovulation. After ejaculation, few sperms reach the outer 1/3 of the fallopian tube (ampulla) aided by contraction of fallopian tube and uterus. The ovum descends down the tube with the help of cilia beating towards the uterus. Sperms undergo physiological changes during their course in the female genital tract. Each sperm contains a large enzyme filled vesicle above its nucleus called acrosome. The interaction of sperm with particular molecules in zona pelucida triggers an acrosomal reaction. This involves the fusion of acrosomal membrane with plasma membrane of the sperm creating pores through which the acrosomal enzymes are released by exocytosis. Those enzymes allow the sperm to digest a pathway through zona pelucida.



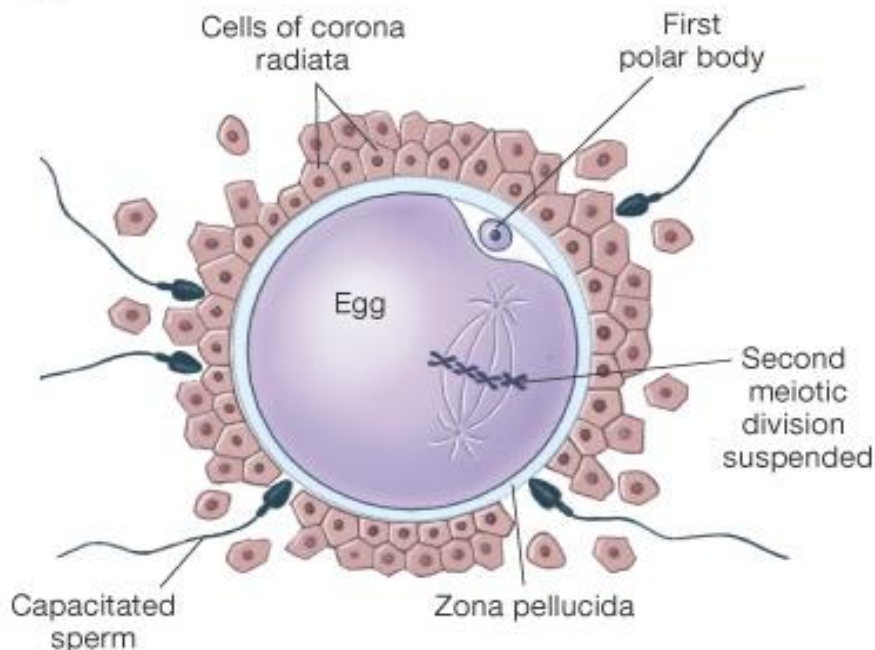
## Oocyte Penetration

1. The **sperm** must penetrate **corona radiata** and **zona pellucida**. This is aided by acrosomal enzymes, hyaluronidase, and proteases.
2. Only one sperm penetrates and activates the oocyte and blocks further sperm penetration.
3. The tail of the sperm degenerates and the head enlarges to form male pronucleus.
4. On penetration of the sperm head, structural changes in membrane of ovum provide further protection against penetration by more sperm (polyspermy)
5. Few hours after sperm penetration, the oocyte is stimulated to complete its second meiotic division to produce mature ovum (23 unpaired chromosomes) and a second polar body which degenerates.
6. Pronucleus from ovum fuses with pronucleus from sperm to form a zygote with 46 chromosomes.
7. One of the 23 chromosomes in ovum is a female chromosome (X chromosome). When it combines with a sperm that carries X chromosome, a female XX fetus is formed.
8. But when the ovum combines with a sperm that contains a y chromosome, a male fetus XY is formed.
9. The centrosome of human zygote is derived from sperm cells. w/out centrosome to form spindle appearance, cell division cannot proceed.

Secondary oocytes ovulated but **not fertilized**. It does not complete its second meiotic division but disintegrates **12-24 hours** after ovulation.

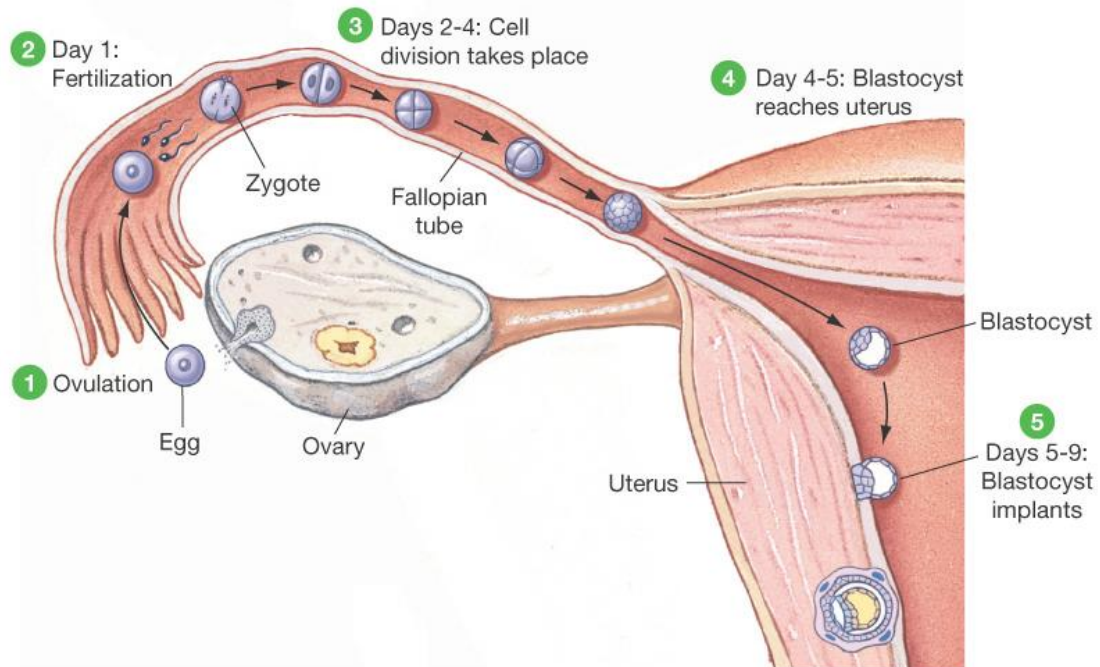
Fertilization cannot occur if intercourse takes place later than one day following ovulation. Sperm can survive up to **3 days** in the female reproductive tract. Fertilization can occur if intercourse takes place within 3 days period prior to day of ovulation.

(b) Capacitated sperm release enzymes from their acrosomes in order to penetrate the cells and zona pellucida surrounding the egg.



### *Cleavage and blastocyst formation*

- At about **36 hours** after fertilization, zygote divides by mitosis causing cleavage into 2 smaller cells.
- Secondary cleavage occurs about **40 hours** after fertilization produces a ball of **8 cells (morula)**
- Morula enters the uterus **3 days after ovulation**. Continued cleavage produces a morula consisting of **32-64 cells** by the 4<sup>th</sup> day. During which time it undergoes changes that convert it into a hollow structure (blastocyst).
- **Blastocyst consists of**
  1. Inner mass cell which becomes fetus
  2. Surrounding chorionic trophoblast cells which become placenta
  3. On 6<sup>th</sup> day of fertilization blastocyst attach to uterine wall with the side containing inner cell mass positioned against the endometrium.
- Blastocyst adheres to endometrium on the 6<sup>th</sup> day and gets implanted on the 12<sup>th</sup> day.
- Trophoblasts produce enzymes that allow the blastocyst to eat its way into endometrium.. This begins the process of implantation and by 7<sup>th</sup> to 10<sup>th</sup> day, the blastocyst is completely buried in endometrium.
- Progesterone is required for implantation and maintaining pregnancy.



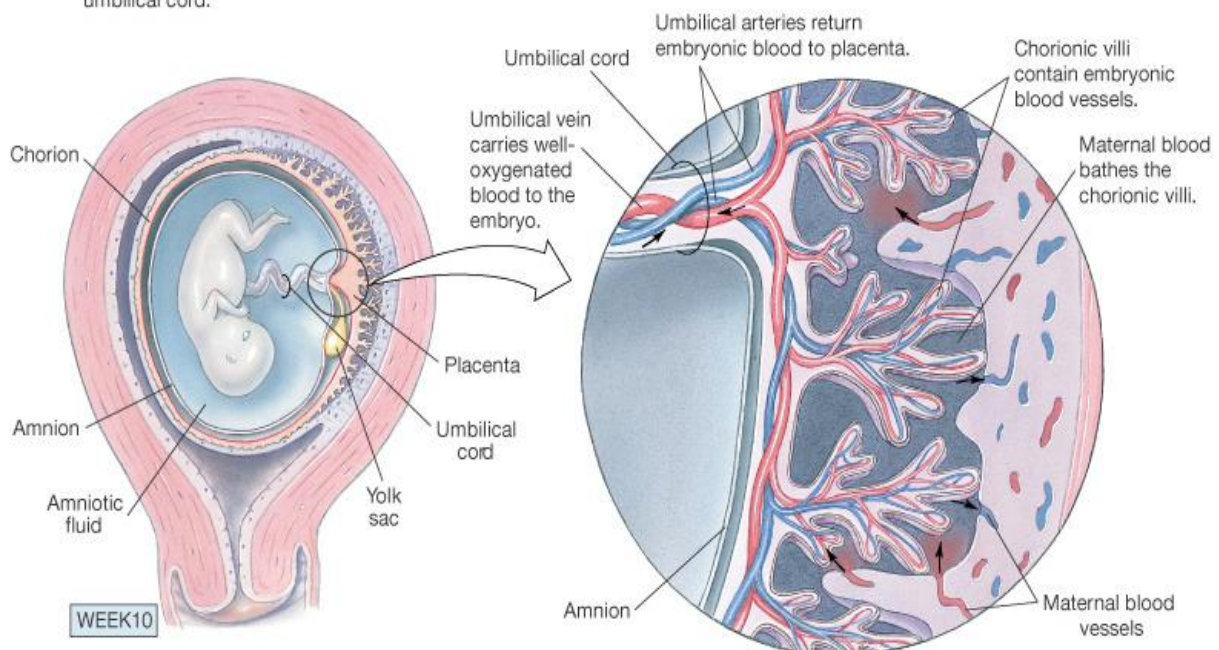
### Functions of Placenta

#### I. Transfer of placenta:

1. Diffusion of O<sub>2</sub> and CO<sub>2</sub> across the placenta membrane
2. Diffusion of food stuff from mother blood to fetal blood. Glucose diffuses down concentration gradient by facilitated diffusion. Protein molecules cannot normally pass however. Immunoglobulins can pass
3. Diffusion of excretory products as urea from fetus back to mother.
4. Placenta has a very high metabolic rate and produces a great variety of enzymes capable of converting hormones and drugs into less active molecules, this way dangerous molecules are prevented from harming fetus.

(a) The developing embryo floats in amniotic fluid. It obtains oxygen and nutrients from the mother through the placenta and umbilical cord.

(b) Some material is exchanged across placental membranes by diffusion, but other material must be transported.



## II. Endocrine Functions

In pregnancy placenta secretes:

1. Human Chorionic Gonadotropin
2. Human Chorionic Somatomamotropin
3. Estrogen
4. Progesterone

### 1-Human Chorionic Gonadotropin

- Secretion from trophoblast cells starts at 8 days after ovulation
- It reaches its maximum 10 weeks after ovulation then decreases to low levels until end of pregnancy.
- Its structure and functions are similar to LH.
- **Functions:**
  - 1) Prevent normal involution of corpus luteum.
  - 2) Causes corpus luteum to grow and secrete estrogen and progesterone which cause endometrium to continue growth and store large amounts of nutrients. After that, corpus involutes and placenta takes its function.
  - 3) Causes fetal testis to secrete testosterone which stimulates development of male sex organs and descent of testis
  - 4) Prevent immunological rejection of implanted embryo.
  - 5) Thyroid stimulating ability like pituitary TSH.
- Early pregnancy test depends on early detection of HCG in the early morning sample urine of pregnant female. Slide test using Ag-Ab reaction.

### 2-Human Chorionic Somatomamotropin

Secreted from placenta at 5<sup>th</sup> week:

- 1) Causes partial development of breast.
- 2) Has lactogenic activity like prolactin.
- 3) Has protein anabolic action similar to GH.
- 4) Decrease glucose utilization by mother by decrease insulin sensitivity, therefore increase blood glucose concentration.
- 5) Promotes release of FFA from fat stores of mother
- 6) Causes polyuria
- 7) This diabetic like effect in the mother helps to ensure a sufficient supply for glucose in the fetus.

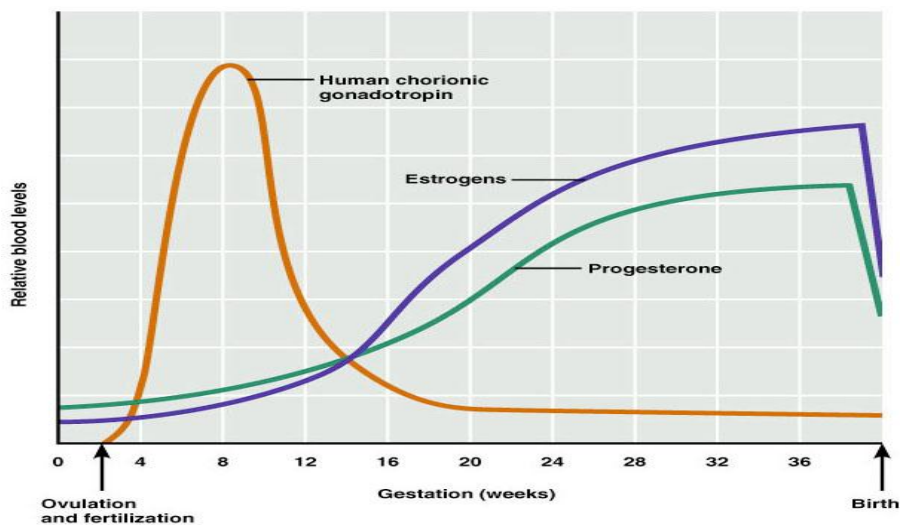
### 3-Estrogen

- a. Estriol is the type secreted from placenta to reach maximum toward end of pregnancy. The precursors are from fetal adrenal that are converted by trophoblasts into estrogens which has several functions:
  - i. Promotes growth and enlargement of uterus to accommodate the fetus.

- ii. Promote growth of breast ductal system.
- iii. Promote growth of mother's external genitalia.
- iv. Relaxation of pelvic joints and ligaments to help passage of fetus through pelvis during labor.

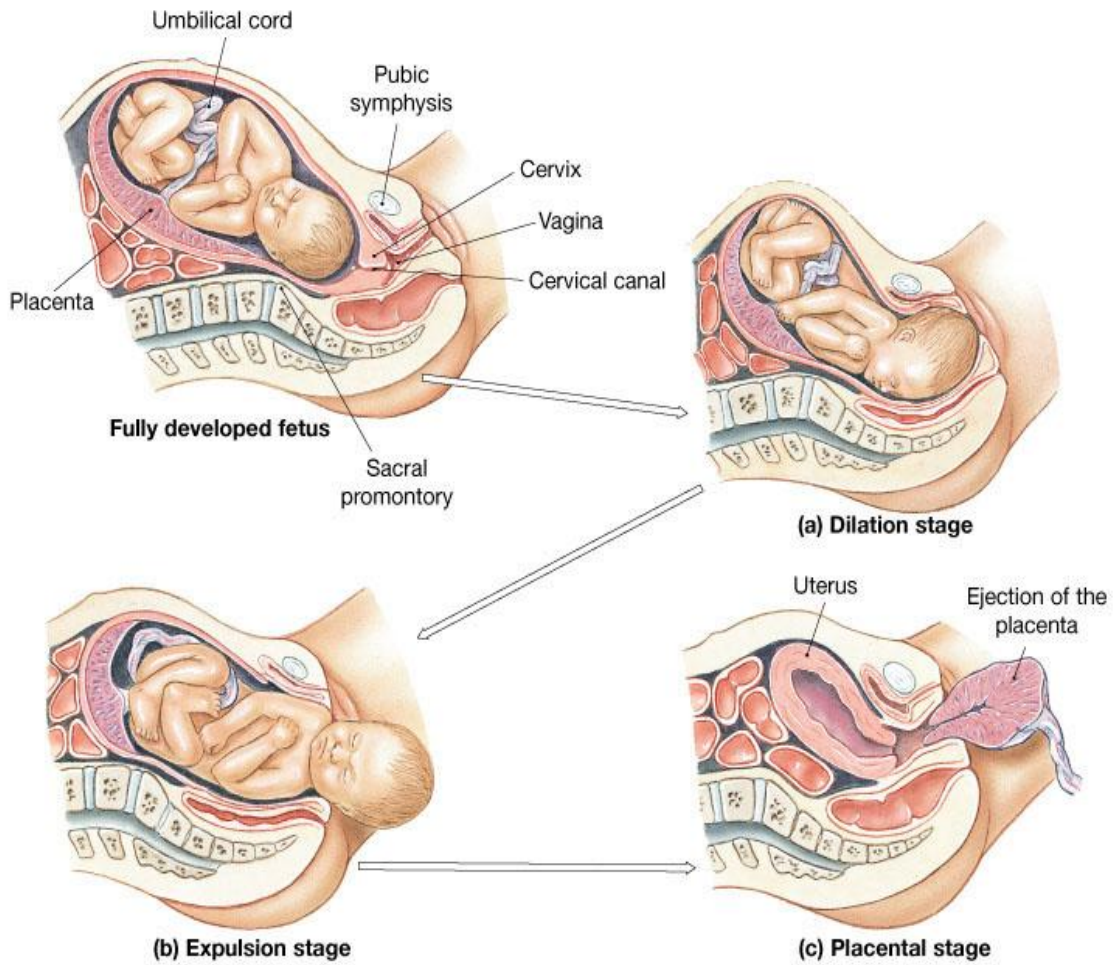
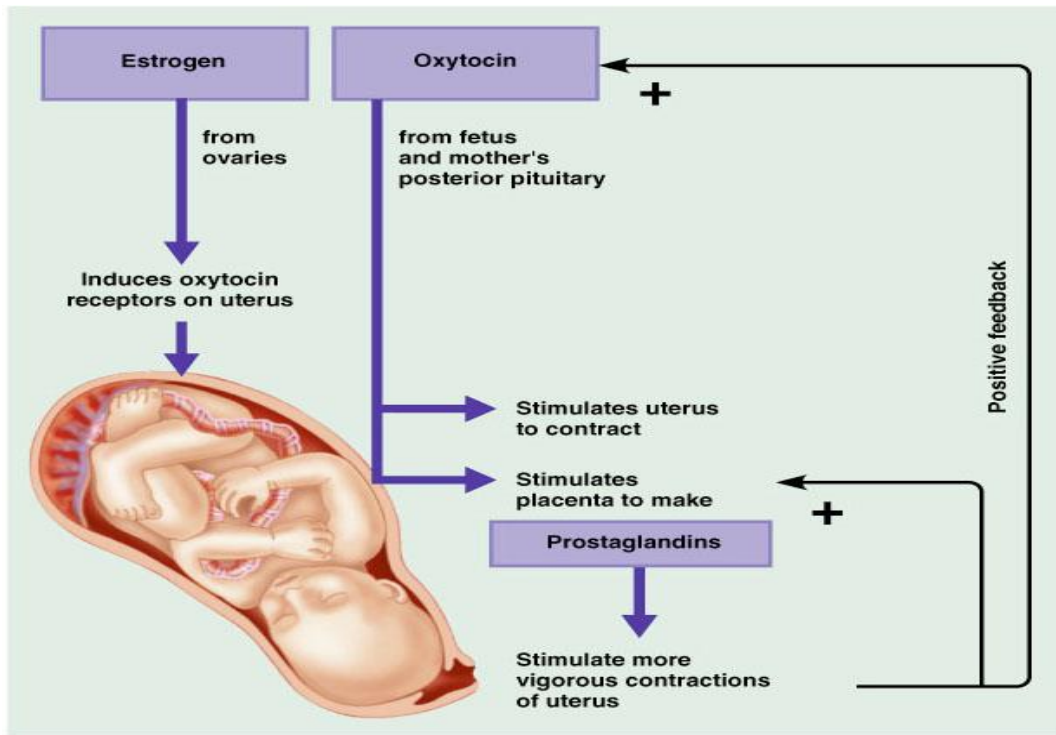
#### 4-Progesterone

- b. Secretes by corpus luteum in early pregnancy, then by placenta starting from 8<sup>th</sup> week onwards.
- c. Reaches its peak value at the end of pregnancy changing estrogen/progesterone ratio in blood 100/1 at beginning of pregnancy to 1/1 toward full term.
  - i. Progesterone increases endometrial nutrient stores of fetal nourishment
  - ii. It decreases contractility, thus prevent spontaneous abortion.
  - iii. It prepares breast for lactation.



#### Parturition

- The process by which the baby is born. At termination of pregnancy, the uterus becomes more excitable until it begins rhythmic contraction that expels the baby.
- **Hormonal factors that increase uterine contractions:**
  - 1) Increase estrogen/progesterone ratio. From 7<sup>th</sup> day onward, estrogen secretion continues to increase while progesterone secretion remains constant. The increase in E/P toward end of pregnancy is responsible for increase uterine contractility. Estrogen activates the myometrium to become more sensitive to oxytocin and prostaglandins
  - 2) The increase rate of oxytocin secretion by neurogenic reflex to posterior pituitary initiated by stretching of uterine cervix.
  - 3) Prostaglandins are found in increased concentration during labor, they increase  $Ca^{2+}$  within myometrial cells and triggers uterine contraction.
- **Mechanical factors**
  - 1) Stretch of uterine musculature that increases contractility.
  - 2) Stretch of cervix that causes transmission of action potential from cervix to uterus.

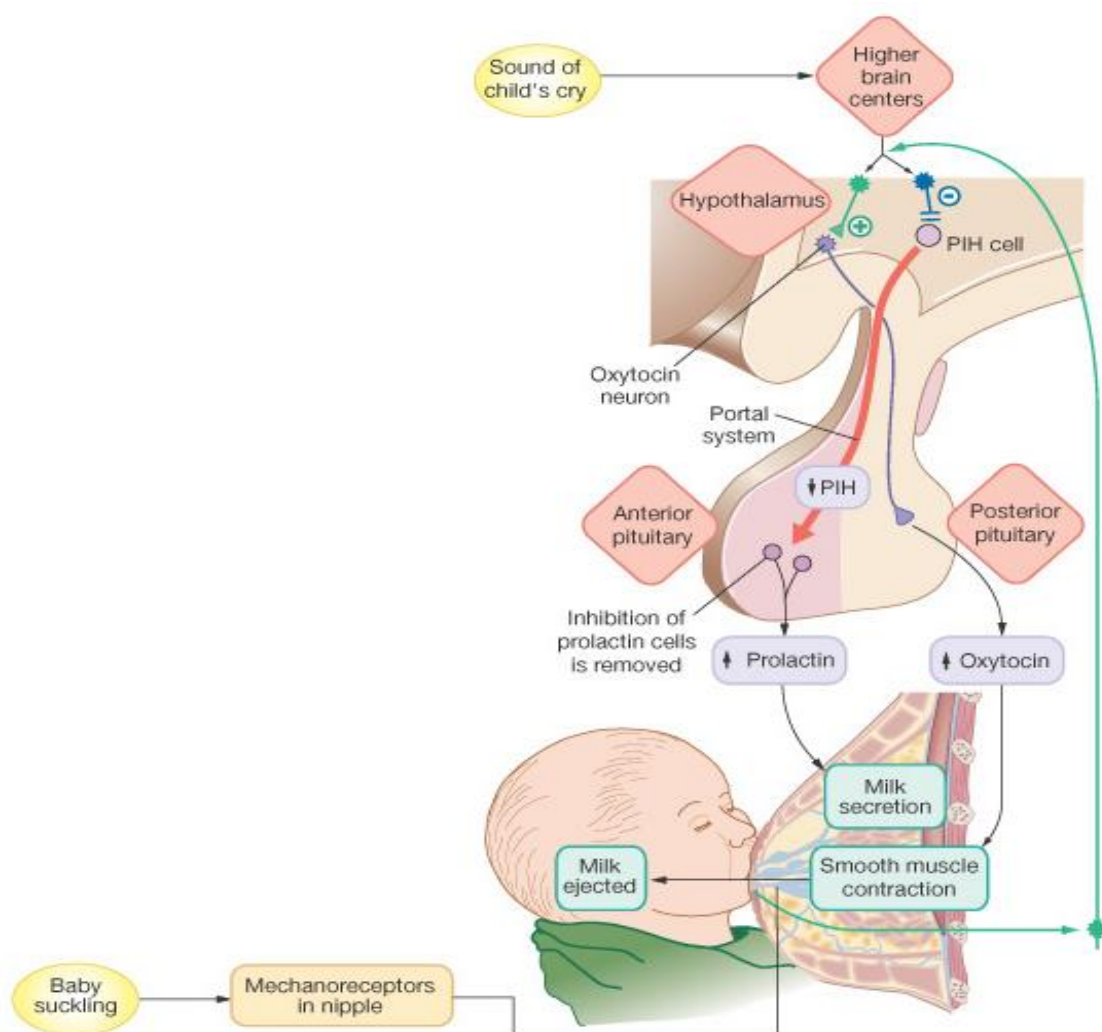


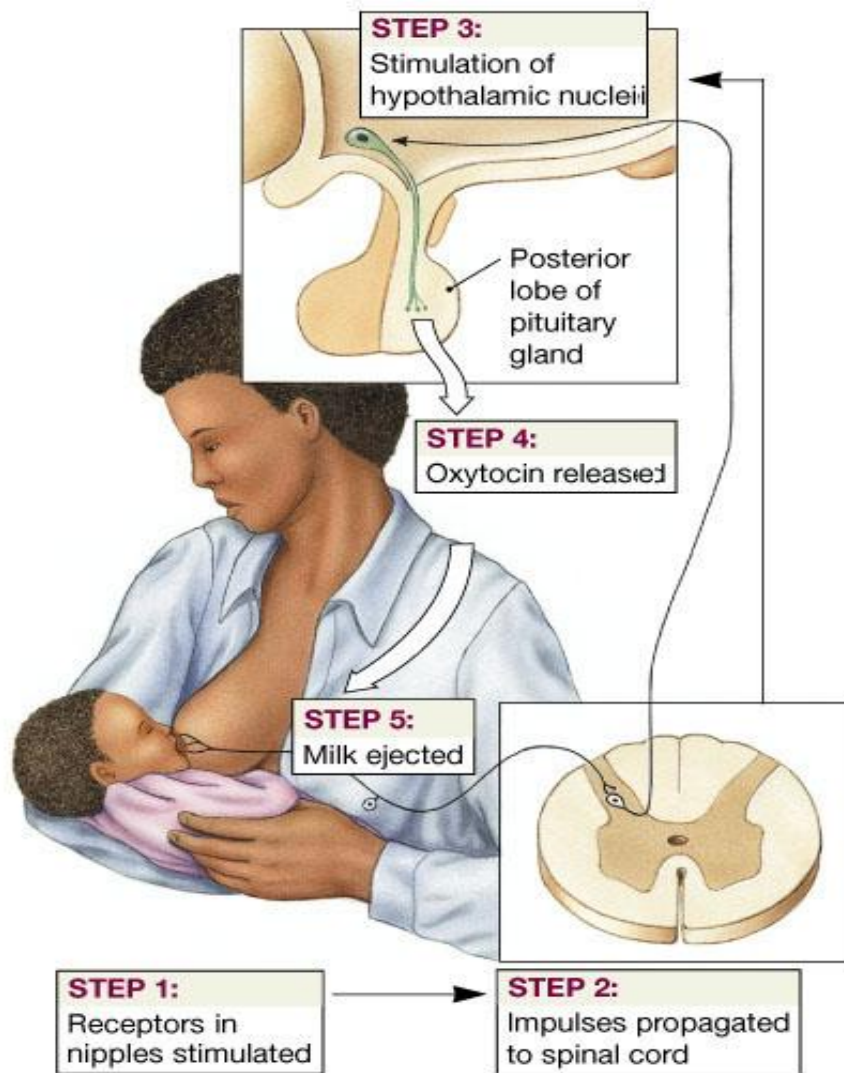


## PHYSIOLOGY OF LACTATION

At puberty, mammary glands develop mainly by effect of:

- 1) Estrogen which causes proliferation of the ducts and deposition of fat with growth of the stroma and development of nipples.
- 2) Progesterone can cause growth of tubules and alveoli with development of secretory characteristics in cells of alveoli.
- 3) Other hormones: GH, insulin, prolactin, TH, adrenal corticosteroids.
- 4) During pregnancy full development of breast occurs by the effect of high level of estrogen and progesterone, HCG as well as insulin, GH, prolactin.
- 5) Milk formation (secretion) stimulated by lactogenic hormones: prolactin and human chorionic somatomamotropin.
- 6) Milk Ejection (letdown) is stimulated by oxytocin which is released by suckling.





### *Initiation of Lactation*

- 1- During pregnancy, very little milk is produced due to high level of estrogen and progesterone which inhibit the action of lactogenic hormones.
- 2 - Milk production in large amounts take 2-3 days after delivery due to sudden loss of estrogen and progesterone from placenta. This allows prolactin to promote milk secretion instead of colostrums that is secreted before parturition.

### *Effect of lactation on ovarian cycle*

- 1- During breast feeding, menstrual cycle usually stops or becomes irregular. Even if menstruation occurs, cycles are anovulatory. This is due to the inhibitory effect of prolactin on GnRH.
- 2- Prolactin decreases the effect of LH & FSH on ovary.
- 3- Prolonged breast feeding can be used for spacing pregnancies.
- 4- Human milk is the most suitable food for infant nutrition as it contains T&B lymphocytes, macrophages, WBC, antibacterial and antiviral substances (IGA, LYSOSOMES)

# ختاماً

إن النجاح والمجد لا يمكن أن ينال بالتفاعس والخمول والكسل، بل لا بد من السعي والجد والاجتهاد للوصول إلى الهدف الذي وضعته، ولا بد أيضاً من الصبر على ما يعترض طريقك من مصاعب وعقبات ومحاولة تذليلها وإزالتها، واحذر من التسويف وتأجيل الأعمال، فإن الوقت يمضي والأعمال كثيرة، فلو جعلتها تتراكم عليك لما استطعت أن تنجز منها شيئاً مما يعني بداية الفشل

2009 A M A N I

عشت معكم أياماً رائعة لن تمحي من ذاكرتي .. وستبقى هذه الأيام شاهداً على اخوة ومحبة في الله جمعني بكم .. احلوني وأنتم بجل .. أسأل الله أن لا يفرقنا .. وأسأل الله لي ولكم التوفيق في cat 4 وأن نحقق به ما لم نستطيع تحقيقه بالـ cats السابقة

2009 A M A N I

اعذرونا إن قصرنا في إيضاح نقطة معينة .. لكن نرجوا أن يكون هذا المرجع سالم من الأخطاء

أن أصبنا فما توفيقنا إلا بالله .. وأن أخطئنا فمن الشيطان ..



دمتم بخير لقائنا سنة ثاني طب إن شاء الله