



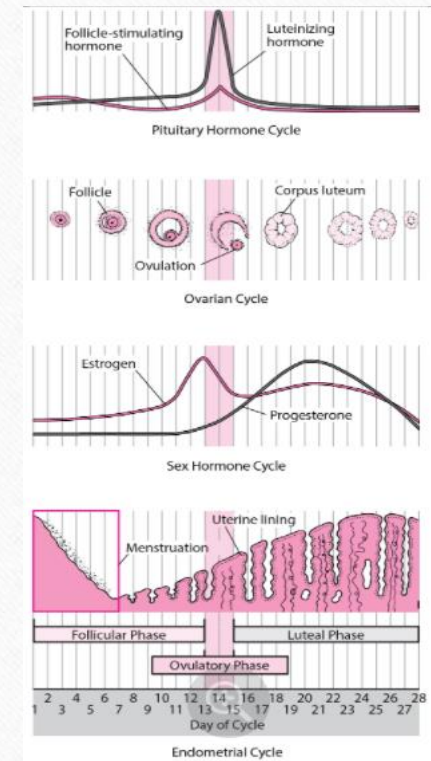
## **Gynecologic problems & herbal treatments**

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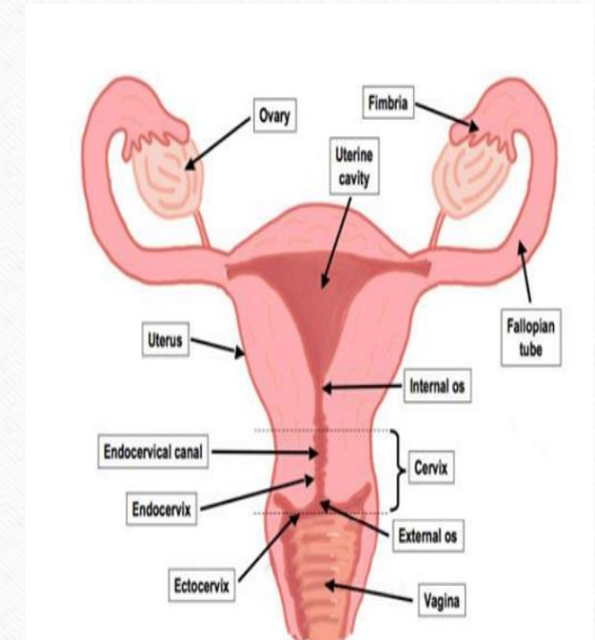
# Outlines

- Female reproductive system & its function
- Cycles
  - Ovarian cycle
  - Menstrual cycle
  - Cervical mucous during menstrual cycle
  - Breast cycle
  - Pituitary hormone cycle
- Hormones
- Gynecologic problems
- Life style based on Persian medicine



# Female reproductive system

- Ovary
  - Oogenesis---oocytes: before birth-by puberty
  - Produces female sex hormones: estrogen, progesterone
- Fallopian tube
  - Fimbriae
  - Infundibulum
  - Ampulla
- Uterus
  - Perimetrium
  - Myometrium
  - Endometrium
- Cervix
  - Endocervix
  - Exocervix
- Vagina



# Function of female reproductive system

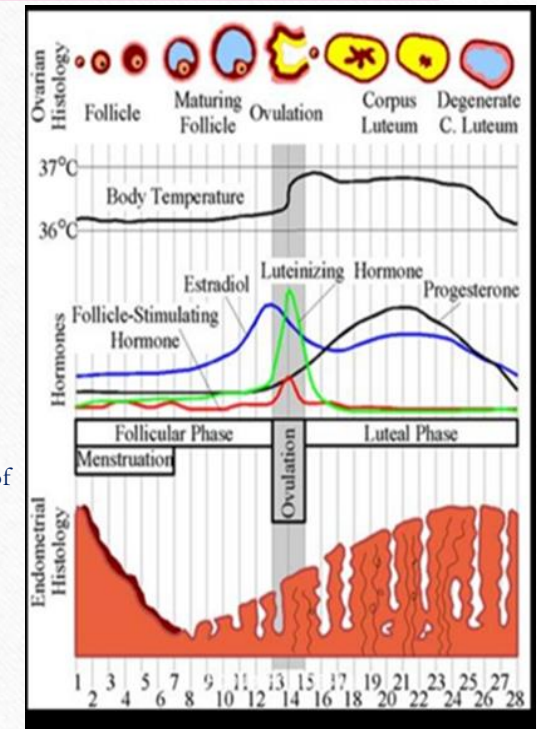
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- Produces and allows oocytes to be fertilized by sperm
- Development of offspring
- Gives birth to a new individual
- The CNS-hypothalamic-pituitary-gonadal target organ axis
  - Luteinizing hormone and follicle-stimulating hormone, which are produced by the pituitary gland:
    - promote ovulation and stimulate the ovaries to produce estrogen and progesterone.
    - Estrogen and progesterone stimulate the uterus and breasts to prepare for possible fertilization
    - The menstrual cycle is regulated by the complex interaction of hormones: luteinizing hormone, follicle-stimulating hormone, and the female sex hormones estrogen and progesterone.
    - Estrogen and progesterone circulate in the bloodstream almost entirely bound to plasma proteins. They stimulate the target organs of the reproductive system (eg, breasts, uterus, vagina). They usually inhibit but, in certain situations (eg, around the time of ovulation), may stimulate gonadotropin secretion.

# OVARIAN CYCLE

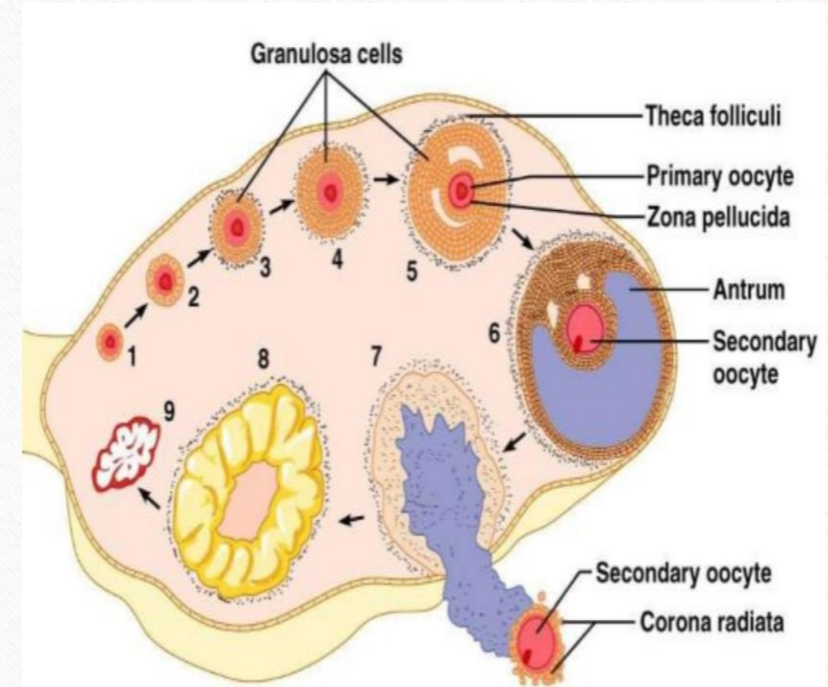
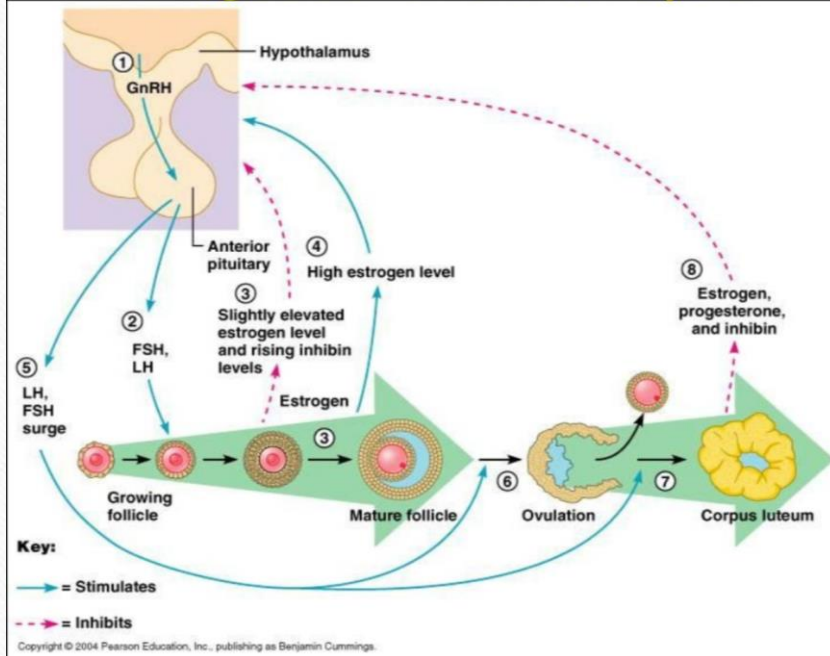
- 28 days
- Follicular phase: 1-13
  - FSH-Development of mature ovum
  - Estrogen release from secondary follicle cavity
- Ovulation: 14: discharge ovum :Egg release between the two ovaries appears to be random. If one ovary is removed, the remaining ovary releases an egg every month.
  - It usually occurs 16 to 32 hours after the surge begins.
  - The estrogen level decreases during the surge, and the progesterone level starts to increase.
  - The surge results in release of the egg (ovulation) and marks the beginning of the next phase.
- 13: 1 fully matured secondary follicle: graafian: estrogen
- 14: EST-LH surge by ant pituitary : graafian rupture: ovulation: release of secondary oocyte

- Luteal phase: 14-28
  - EST->Decrease FSH- other follicle atresia/Scar tissue,
  - Progesterone release by
  - 15-25: Graafian follicle degeneration: Corpus luteum: progesterone & estrogen: endometrial development
  - 26 : if no fertilization :corpus luteum degeneration in the lack of hCG from embryo
  - 26: if fertilization: corpus luteum stimulation with hCG : 2-3 m: high level of progesterone & estrogen to maintain pregnancy



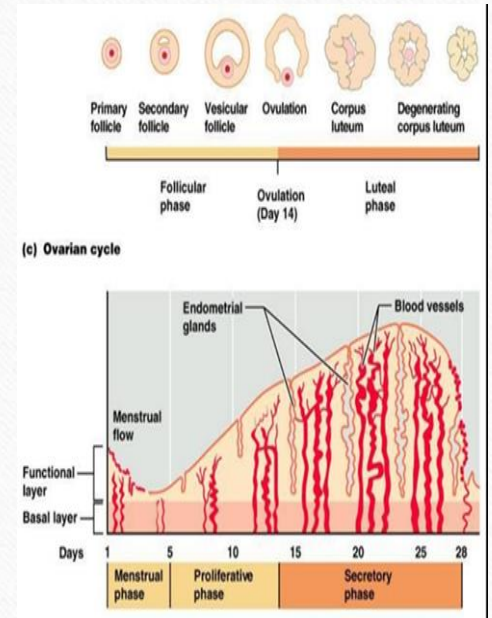
# OVARIAN CYCLE

## 4. Regulation of Ovarian Cycle



# Menstrual cycle

- Simultaneously with ovarian cycle: 28 days
- Menstruation phase: 1-6 days
  - Menses :Blood 75% A, 25% V, Mucus, Secondary oocyte, Stratum functionalis tissue. Menstrual blood, unlike blood resulting from an injury, usually does not clot unless the bleeding is very heavy.
- Proliferative: preovulatory phase: 7-13
  - Secondary & mature follicle: estrogen: to thicken endometrium
- Secretory: post ovulatory phase: 15-28
  - Corpus luteum: estrogen and progesterone: to thicken & vascularization of endometrium
  - Uterine glands will dilate and secrete uterine milk within the secretory phase of the cycle.
    - essential for survival and development of the embryo or fetus



# Abnormal Menstrual cycle

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- Duration
  - <21d, >35d, 6m amenorrhea in irregular menses and 3 m in regular menses
- Menstruation
  - <3d, >10 d
- Bleeding
  - Changing pad every 2 h or nightly, weakness, clot>2.5 cm



# Cervical mucous during menstrual cycle

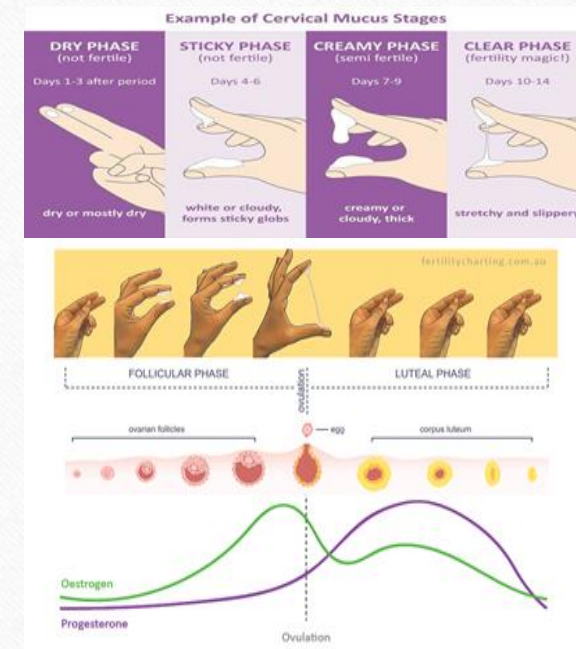
- Cervical mucus before ovulation  
Dilute filamentous mucus

- increasing estradiol levels increase cervical vascularity and edema and cervical mucus quantity, elasticity, and salt (sodium chloride or potassium chloride) concentration. The external os opens slightly and fills with mucus at ovulation.

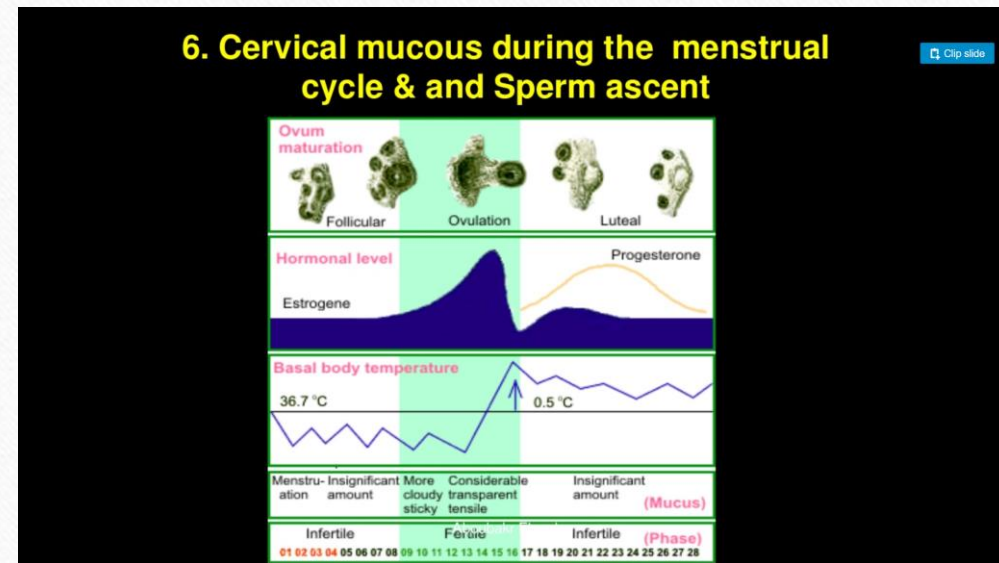
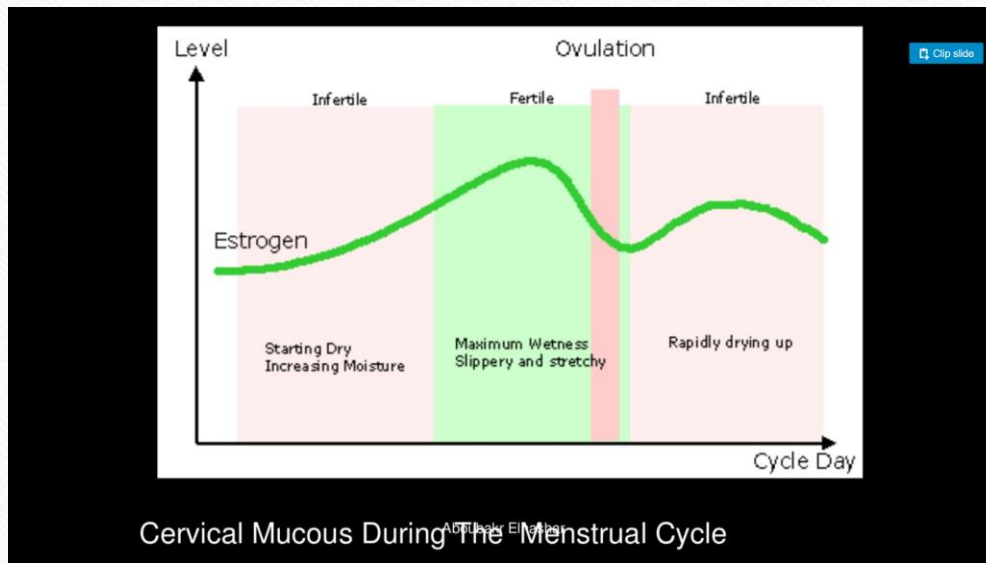
- Cervical mucus in mid cycle

- Cervical mucus at luteal phase

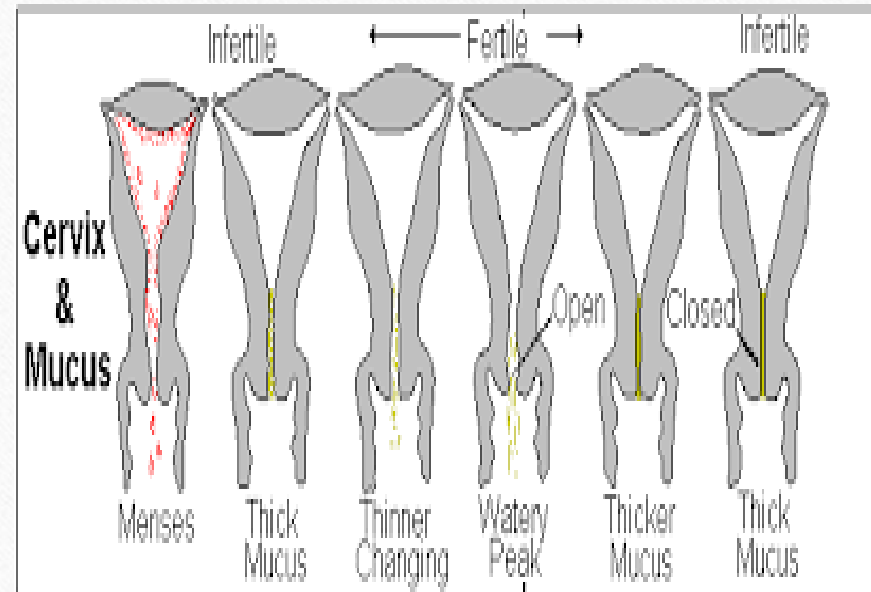
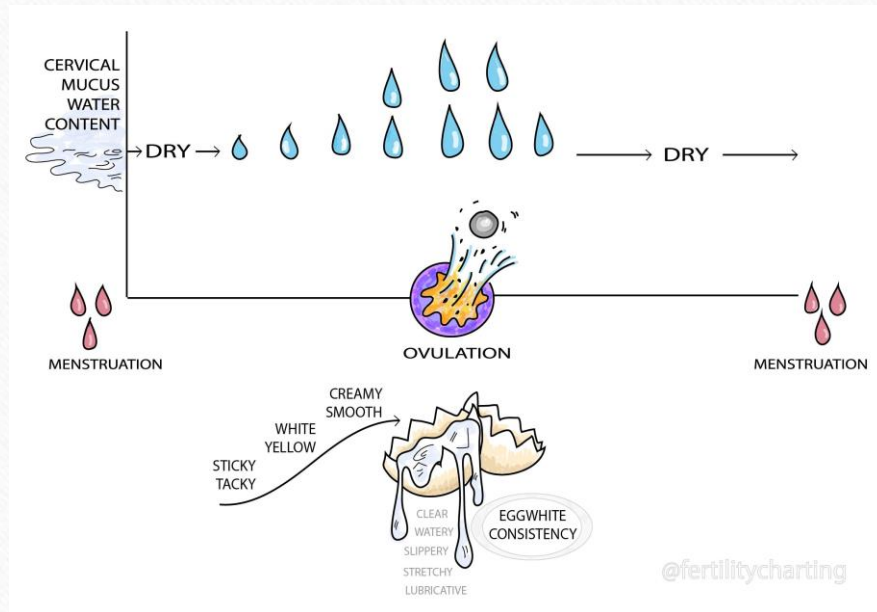
- increasing progesterone levels make the cervical mucus thicker and less elastic, decreasing success of sperm transport. so that sperm or bacteria are less likely to enter the uterus



# Cervical mucous during menstrual cycle

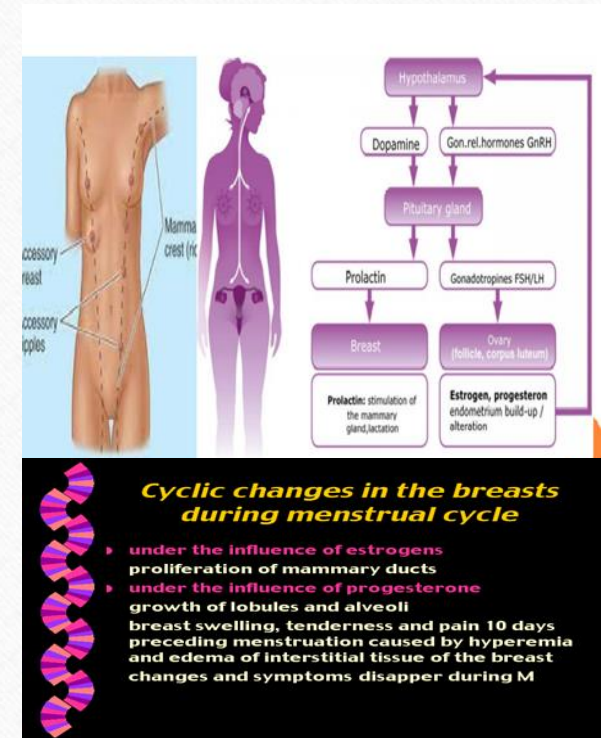


# Cervical mucous during menstrual cycle



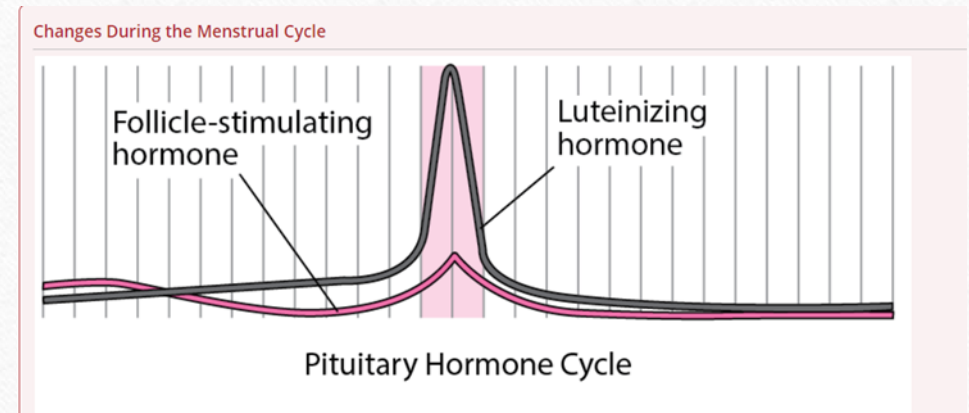
# BREAST CYCLE

- Estrogen phase
  - Proliferation of mammary ducts
- Progesterone phase
  - The growth of lobules and alveoli



# Hormones

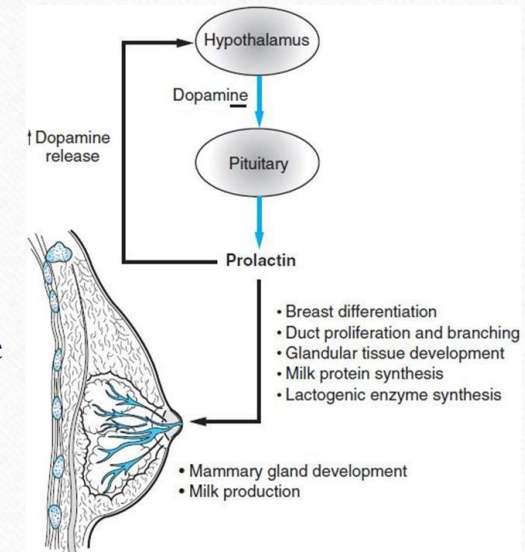
- Prolactin
- TSH
- FSH , LH
- Estrogen
- Progesterone
- 17 OHProgesterone
- Androgens :
  - Testestrone
  - DHEAS



# Hormones

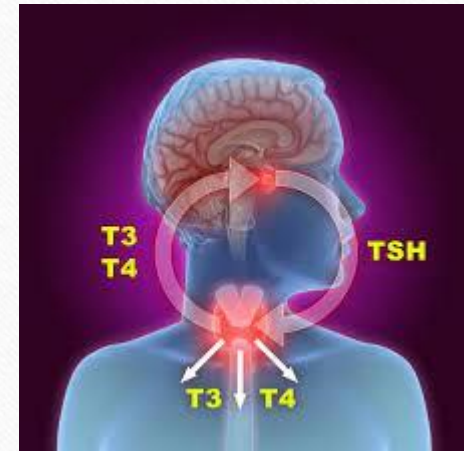
- Prolactin

- Ant pituitary
- Lactation
- <20 ng/ml: pre menopausal
- <12 ng/ml: post menopausal
- Detection: late morning, fasting, after 60 min rest, not in late follicular phase
- Hyposecretion: rare: pituitary necrosis, infection
- Hypersecretion : idiopathic, physiologic, pathologic, pharmacologic
  - Clinical condition: galactorrhea, oligomenorrhea, anovulation, infertility, hirsutism



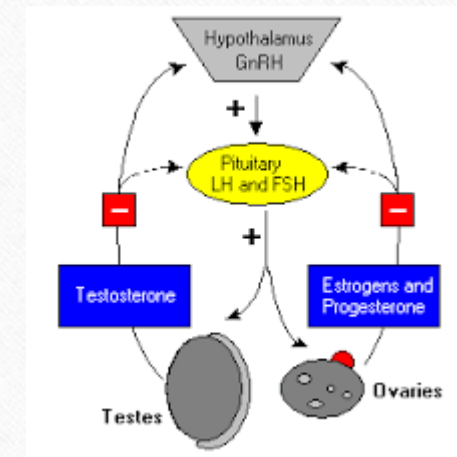
# Hormones

- TSH
  - Subclinical hypothyroidism: increased TSH, nl free T4
  - Clinical condition
    - oligomenorrhea, amenorrhea, menorrhagia, anovulation, subfertility



# Hormones

- FSH , LH
  - Ant pituitary
  - Normal values
    - Adult FSH: 5-10mIU/ml- 2yimes in mid cycle
    - Adult LH: 5-20mIU/ml- 3 times in mid cycle
  - Clinical uses
    - Hypogonadotropic state: prepubertal, pituitary disorder: <5
    - Hypergonadotropic state: post menopause, ovarian failure: >40
    - PCOS: LH/FSH: 2/1
    - Testing for ovulation function, detection of ovulation
    - Diagnosis of the cause of precocious puberty
    - Diagnosis of the cause of amenorrhea



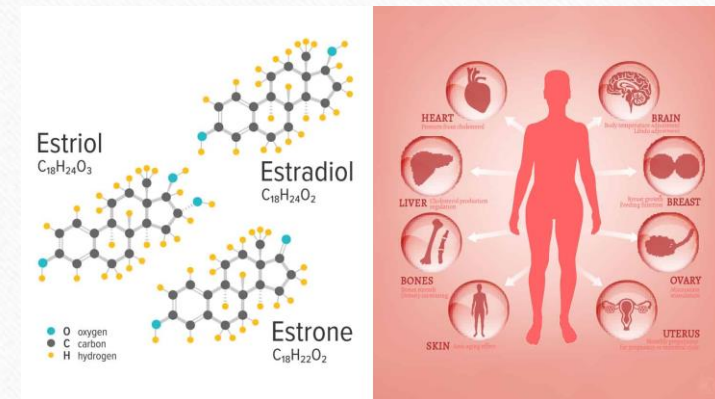


# Hormones

- Estrogen

3 out of 30 estrogen are used in clinical practice

- E1: Estrone: highest concentration in post menopausal
- E2: Estradiol: entirely secreted by ovary: most abundant in premenopausal female, most potent
- E3: Estriol



# Hormones

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- Estrogen
  - Synthesized from cholesterol
  - Produce primarily by ovaries, placenta and corpus luteum/ adrenal
  - Metabolized by the liver
  - Excreted in the bile, feces and the urine(horses)

# Hormones

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- Estrogen
  - E2 Rises during the second half of follicular phase & reach a peak 24 h before LH surge and 36 h before ovulation
  - After LH surge E2 drops to preovulatory levels, but then rises slightly to 100-300 pg/ml during luteal phase
  - E2 nl levels
    - Follicular phase: 25-27
    - Midcycle peak: 200-600
    - Luteal phase: 100-300
    - Postmenopausal: 5-25

# Hormones

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- Estrogen
  - Clinical application
    - E secreting tumor: granulosa theca cell tumor
    - Classification of hypogonadism
    - Test for ovarian reserve
    - Monitoring super ovulation in ART
    - Indication of downregulation
    - Monitoring induction ovulation with HMG

# Hormones

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- Function of Estrogen
  - Maturation, growth & development of reproductive system: Growth of uterus, fallopian tubes & vagina
  - Estrogen deficiency: atrophic changes in female reproductive tract
  - Stimulation of normal physiological process of reproductive tract
    - Uterine muscle growth
    - Development of endometrial lining of uterus
    - Increase the vascularity of uterus
  - Induction of behavioral estrus
  - Dilation of cervix, liquefaction of mucous plug
  - Making uterus less susceptible to infection
  - Increase vaginal lubrication
- Sex organs
  - Pubertal changes
  - Menstruation in anovulatory cycles
  - enhances sperm penetration
- Secondary sex characters
  - Breast: proliferation of ductus & stroma, accumulation of fat
  - Pubic & axillary hair appear
  - Feminine body contour and behavior

# Hormones

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- Function of Estrogen
- Metabolic
  - Anabolic: pubertal growth spurt in boys & girls
  - Bone mass: retard bone resorption, Protects bone health, Reduce bone resorption, increase bone formation, promotes fusion of epiphyses
  - Water & salt retention: edema, blood pressure rise in prolonged uses
  - Glucose tolerance: high doses
  - Lipid profile: Keeps cholesterol in control: decrease of LDL, Increase HDL , TG
  - Blood coagulability: increased
  - Vascular endothelium: NO, PGI2: vasodilation
  - Gall bladder: Litogenicity: increase cholesterol, decrease of bile salt
  - HBG: increased plasma SHBG, TBG, CBG

# Hormones

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- Progesterone
  - In the serum: 3% is free
  - Value:
    - Low prior to midcycle gonadotrophin surge, begin to rise shortly after that, reaching peak level during the middle of luteal phase(8 d after LH peak), then a progressive decrease happens
    - Follicular phase:<1
    - Luteal phase: 5-20
    - Postmenopausal: <1
  - Clinical application
    - Diagnosis of ovulation
    - Diagnosis of corpus luteal dysfunction

# Hormones

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- Function of Progestin
- Sex organs
  - Uterus: secretory changes in the estrogen primed endothelium: hyperemia, tortuosity of glands, increased secretion
  - During pregnancy: decidual changes & sensitivity of myometrium to oxytocin decreased
  - Cervix: scanty(low) and cellular secretion: hostile to sperm penetration
  - Vagina: pregnancy like changes
- Secondary sex characters
  - Breast:
    - Luteal phase exposure: cyclic epithelial proliferation
    - Continuous exposure: prepare breast for lactation
    - HRR: increases risk of breast malignancy
  - CNS: sedative in high concentration
  - Pituitary
    - Weak inhibitor of gonadotrophin secretion
  - Body temperature: slight rise: 0.5
  - Respiration
  - Metabolism



# HORMONS

	Estrogen	Progesterone
Vagina	Slight mucus secretion, hyperemia, oedema	Slight mucus secretion, paleness, exfoliation
Cervix	Relaxation, liquefaction of mucus plug	Closure, formation of mucus plug
Uterus	Secretion of PGF2 alfa, PGE2 Uterine gland development Sensitization to oxytocin	Inhibition of PGF2 alfa, PGE2 Uterine gland secretion Sensitization to oxytocin Decreased uterine motility
Fallopian tube	Increased motility & cilia activity	Decreased motility Increased secretion
Mammary gland	Stimulates mammary duct development	Stimulates lobulo-alveolar development

# HORMONS



## Estrogen: Side Effects

Clip slide

Population Groups	Side Effects
Males	Suppression of libido, gynaecomastia and feminization
Children	Fusion of epiphyses and reduction of adult stature
Postmenopausal women/ on HRT	Risk of irregular bleeding and endometrial carcinoma
Existing Breast cancer	Growth of existing breast cancer
Women under long term estrogen therapy	Increased incidence of gallstones, benign hepatoma
Co-morbidity	Worsening of Migraine, epilepsy, endometriosis
Pregnant Women(esp. first trimester)	Vaginal and cervical carcinoma in female offspring in childhood or early adulthood



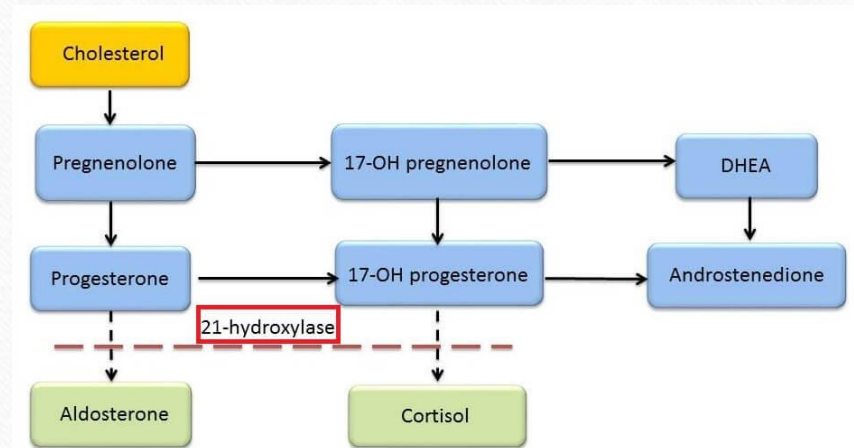
## Progestins: Side Effects

Clip slide

- General:
  - Breast engorgement, headache, rise in body temperature, edema, esophageal reflux, acne mood swings with higher doses
  - Irregular bleeding or amenorrhoea on continuous administration
  - Painful injection
- 19-nortestosterone derivatives:
  - Lowers plasma HDL levels → promotes atherogenesis
  - Impaired glucose tolerance, precipitate diabetes
- Long term administration(HRT): Increase risk of breast cancer
- Early pregnancy: Masculinization of female foetus and other congenital abnormality

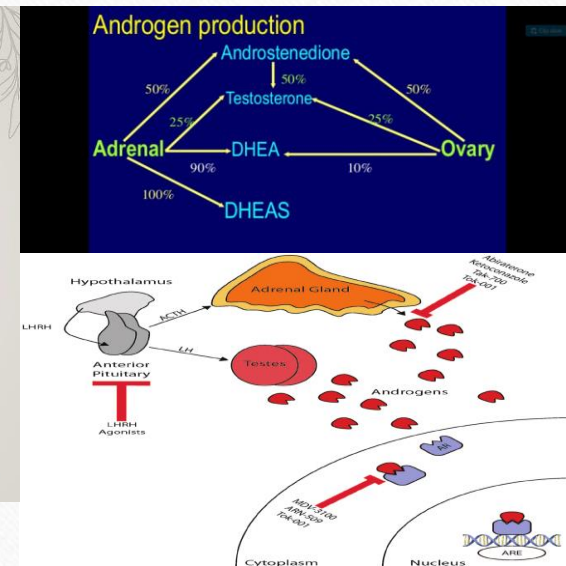
# Hormones

- 17 OHProgestrone: adrenal
  - Increased in congenital adrenal hyperplasia
  - Clinical application:
    - Hirsutism
    - Ambiguous genitalia



# Hormones

- **Androgens : total testosterone, DHEAS**
  - Pubic and axillary hair growth may be stimulated by the adrenal androgens dehydroepiandrosterone (DHEA) and DHEA sulfate;
  - production of these androgens increases several years before puberty in a process called adrenarche.
- **NI Values**
- **Testosterone: clinical: in hirsutism**
  - Premenopausal: 20-80
  - Postmenopausal: 15-70
- **Androstenedione**
  - Premenopausal: 60-300
  - Postmenopausal: 30-150
- **DHEAS > 2 in PCOS & hirsutism**



# Common gynecological problems

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- Uterine:
  - Menstrual problems
    - Abnormal vaginal bleeding
    - Dysfunctional uterine bleeding
    - Amenorrhea
    - Dysmenorrhea
  - Others : myomatous polyps, endometriosis
- Ovary
  - PCOS
  - Cyst
- Cervix
- Vagina
  - Vaginal discharge and infection
- Puberty
- Fertility
- Pregnancy
- Infection
- Post menopausal problems
  - Atrophic vaginitis
  - Malignancy
- Psychosexual problem
- Malignancy

# Persian medicine Life style based

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- Weather: avoid wet & cold
- Nutrition : avoid cold, spicy, salty, sour
- Detoxification: constipation, intercourse
- Sleep & wakefulness: melatonin
- Exercise : circulation
- Emotional stress: deep breath

# خلاصه

## • سیکل تخمدانی

## • سیکل رحمی

فاز لوتئال	تخمک گذاری	فاز فولیکولر	تخمدان	فاز ترشحي پروژسترونی	فاز تکثیری استروژنی	فاز قاعدگی	رحم
جسم زرد: (باقیمانده فولیکول): تولید پروژسترون و کمی استروژن در عدم بارداری: افت این دو و ریزش لایه داخلی رحم در صورت بارداری: حفظ حاملگی ↑ اندروژن	پیک LH : آزاد سازی تخمک توسط فولیکول غالب از بین 5-20 فولیکول تخمک-لوله-رحم: 24-36 ساعت قدرت بارور شدن با اسپرم را دارد	تحت اثر FSH رشد فولیکول حاوی تخمک : تولید <u>استروژن</u> و کمی پروژسترون: تکثیر رحم رشد فولیکول ↑ رسپتور LH ↓ FSH و اتروپی سایر فولیکولها		استروژن و پروژسترون: ↑ ضخامت لایه داخلی رحم برای لانه گزینی: uterine milk from fertilization to implantation	↑ استروژن ↑ ضخامت لایه داخلی رحم برای لانه گزینی	در عدم بارداری: قاعدگی ↓ استروژن پروژسترون ریزش اندومتر + 75% خون شریانی + 25% خون وریدی: 40 سی سی + 35 سی سی مایع سروزی	

# خلاصه

## • سیکل واژن و سرویکس

## • سیکل پستان

واژن و سرویکس	فاز استروژنی یا تکثیری	فاز پروژسترونی	پستان	فاز استروژنی	فاز پروژسترونی
	اپیتلیال شاخی و روگای مشخص واژن موکوس ترشحاتی رشته ای رقیق و قلیایی هدایت اسپرم	لکوره سفید و ارتشاح گلبول سفید ترشحات غلیظتر		تکثیر مجاری شیری و افزایش چربی پستان درد و تورم و احتقان	رشد توبولها و تکثیر و بزرگ شدن الوئولها امادگی برای شیردهی درد و سنگینی

نکته: ترشحات رحم از زمان لقاح تا لانه گزینی را Uterine milk گویند



# خلاصه

- استروژن
  - استرادیول E2
    - تولید در تخمدانها
    - بیشترین قدرت متابولیک
    - پیک ان قبل از تخمک گذاری
  - استرون E1
    - بیشتر از بافت چربی محیطی و کمی از تخمدان
  - استریول E3
    - فرآورده اکسداثیو از استرادیول و استرون در کبد
    - استروژن اصلی جفت
  - تجزیه و دفع استروژنها عمدتاً توسط کبد
  - اثر بر تخلیه نورونی مغز، افزایش NO، افزایش خونرسانی رحم
- پروژستین
  - تولید عمده ان از تخمدانها در فاز لوتئال
  - تولید جزئی از ادرنال
  - در کبد تجزیه می شود
  - از ادرار دفع می شود
- اندروژنهای فوق کلیوی
  - تأثیر بیشتری بر روند توزیع مو در نواحی زیر بغل و پوبیس دارند

