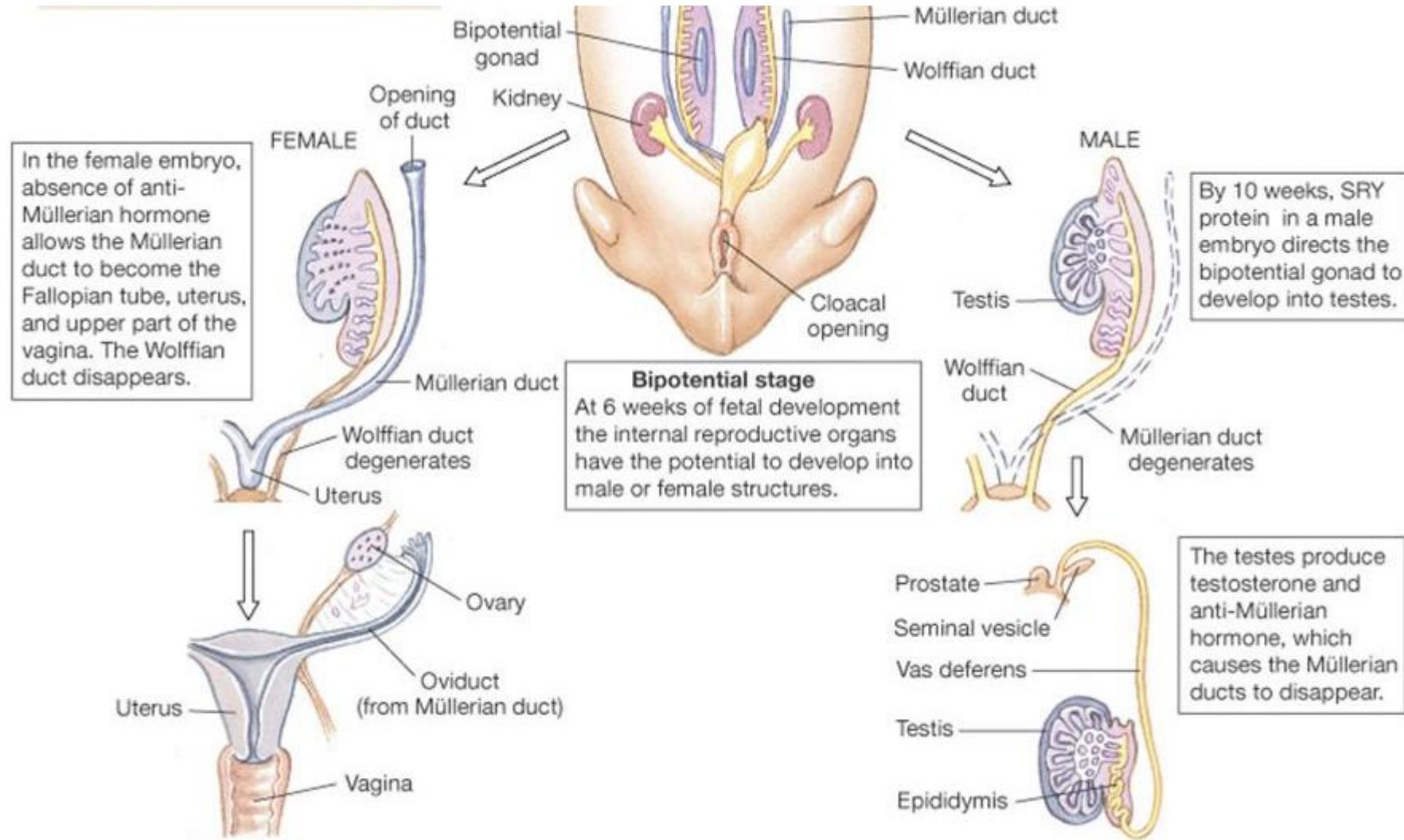


Gonadal hormones

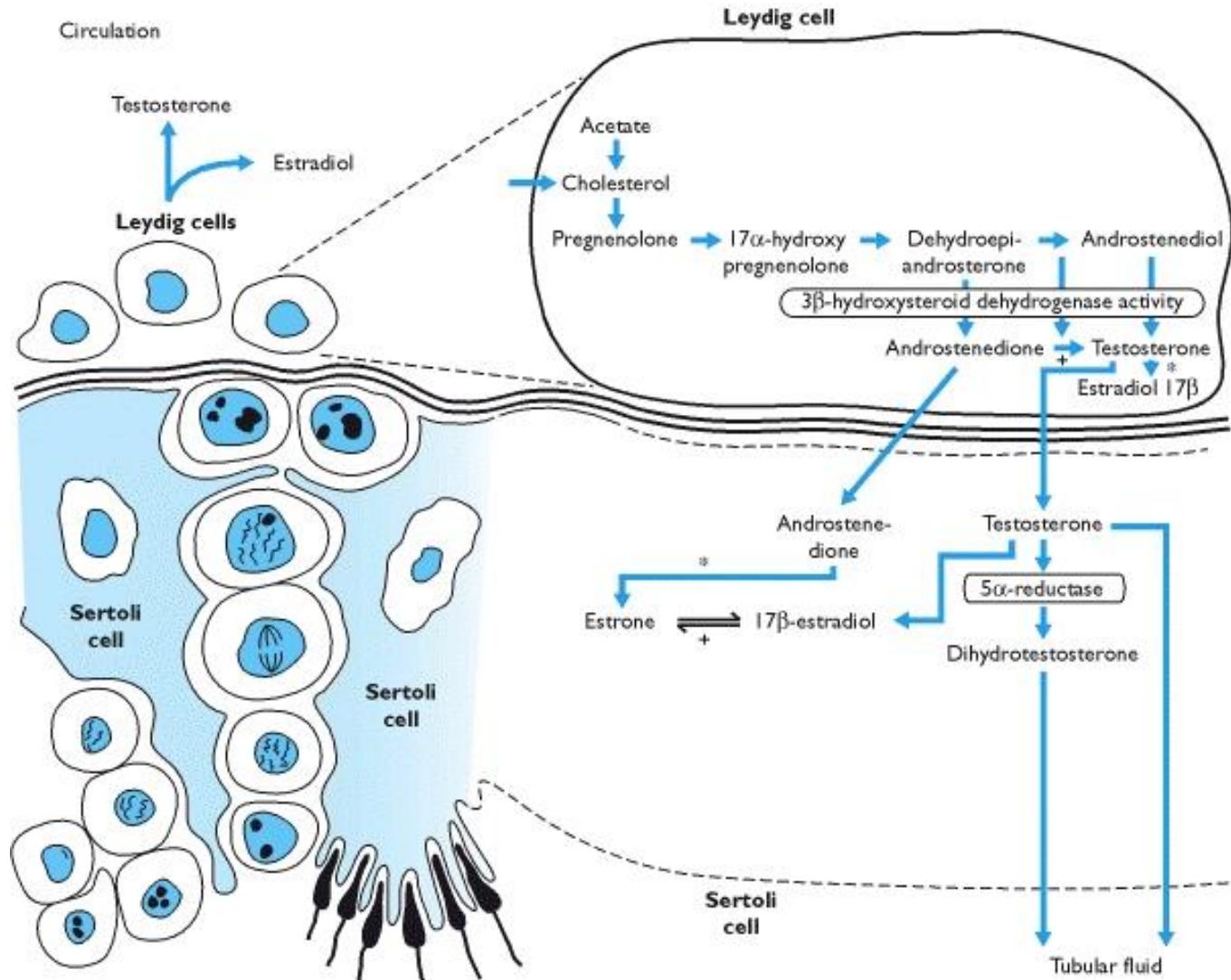
Mgr. Emese Renczés, PhD.

renczes.emese@gmail.com

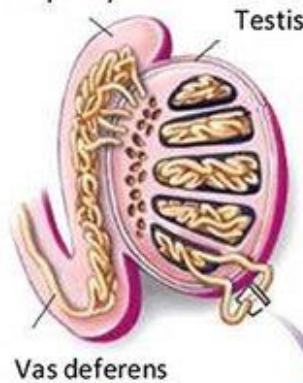
Sexual differentiation



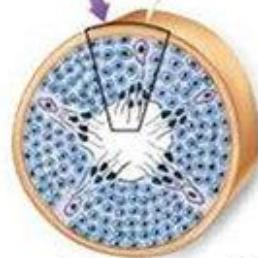
Male gonads



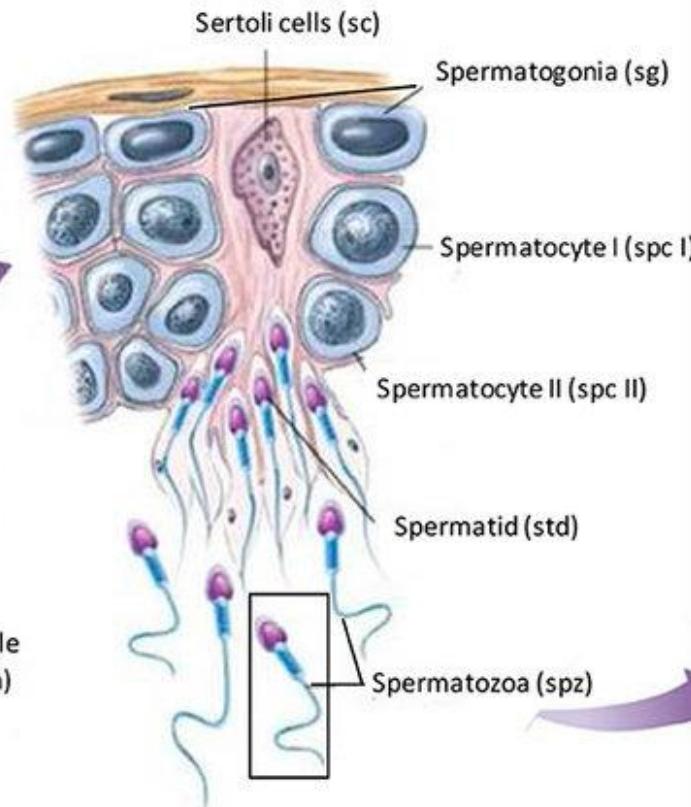
Epididymis



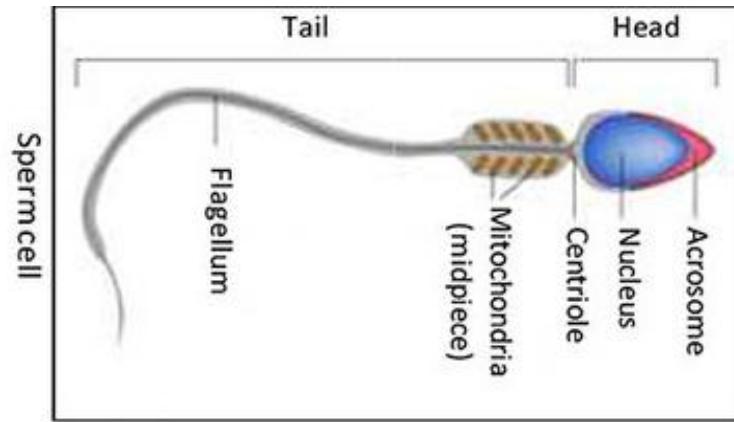
Vas deferens



Seminiferous tubule
(transverse section)

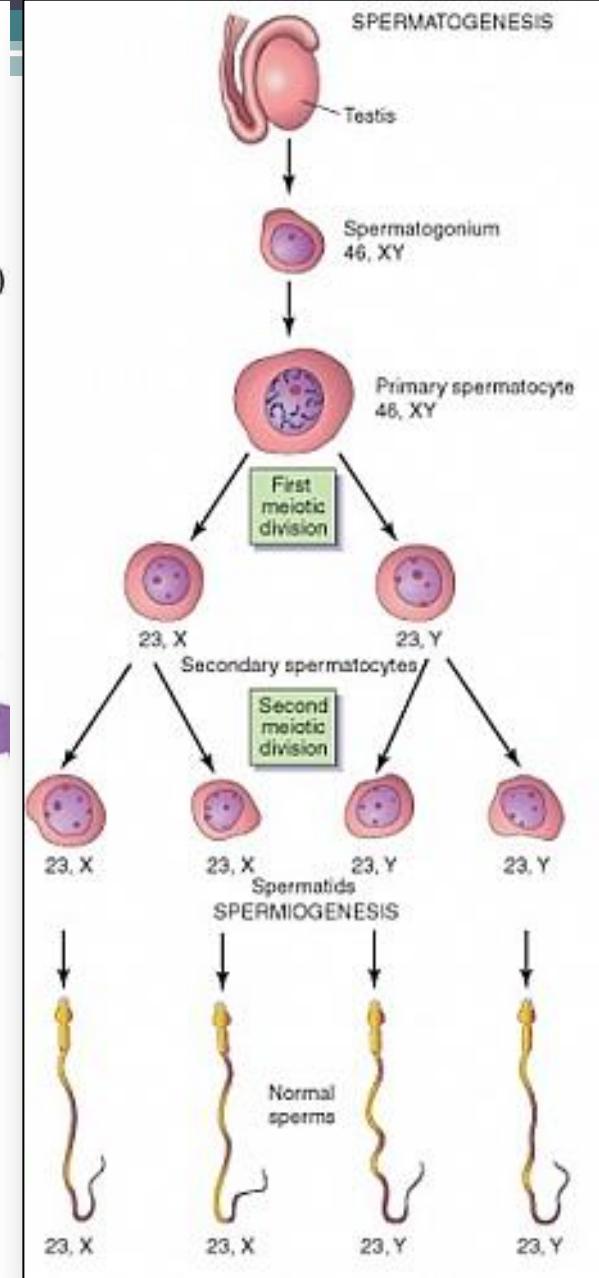


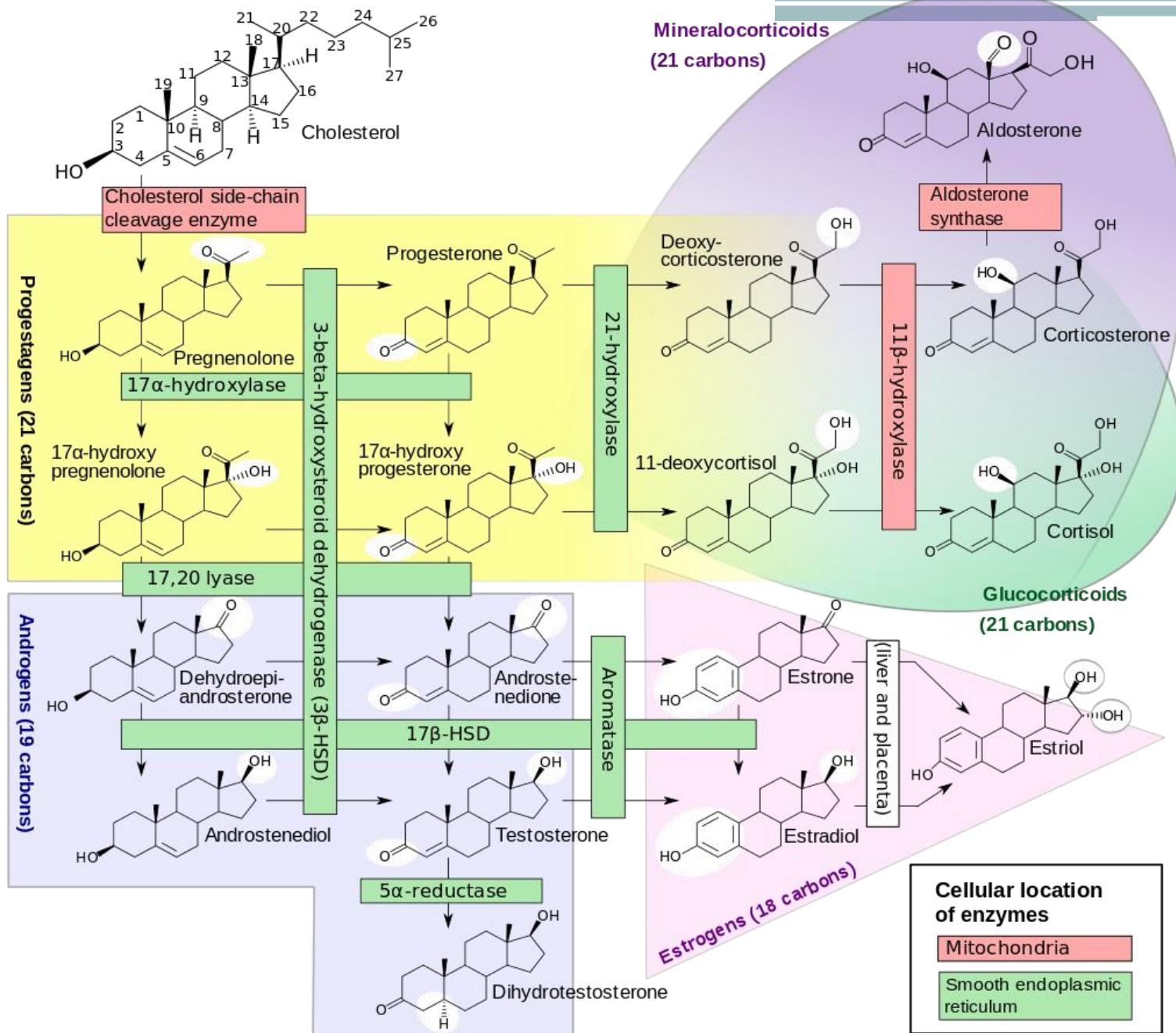
Tail Head



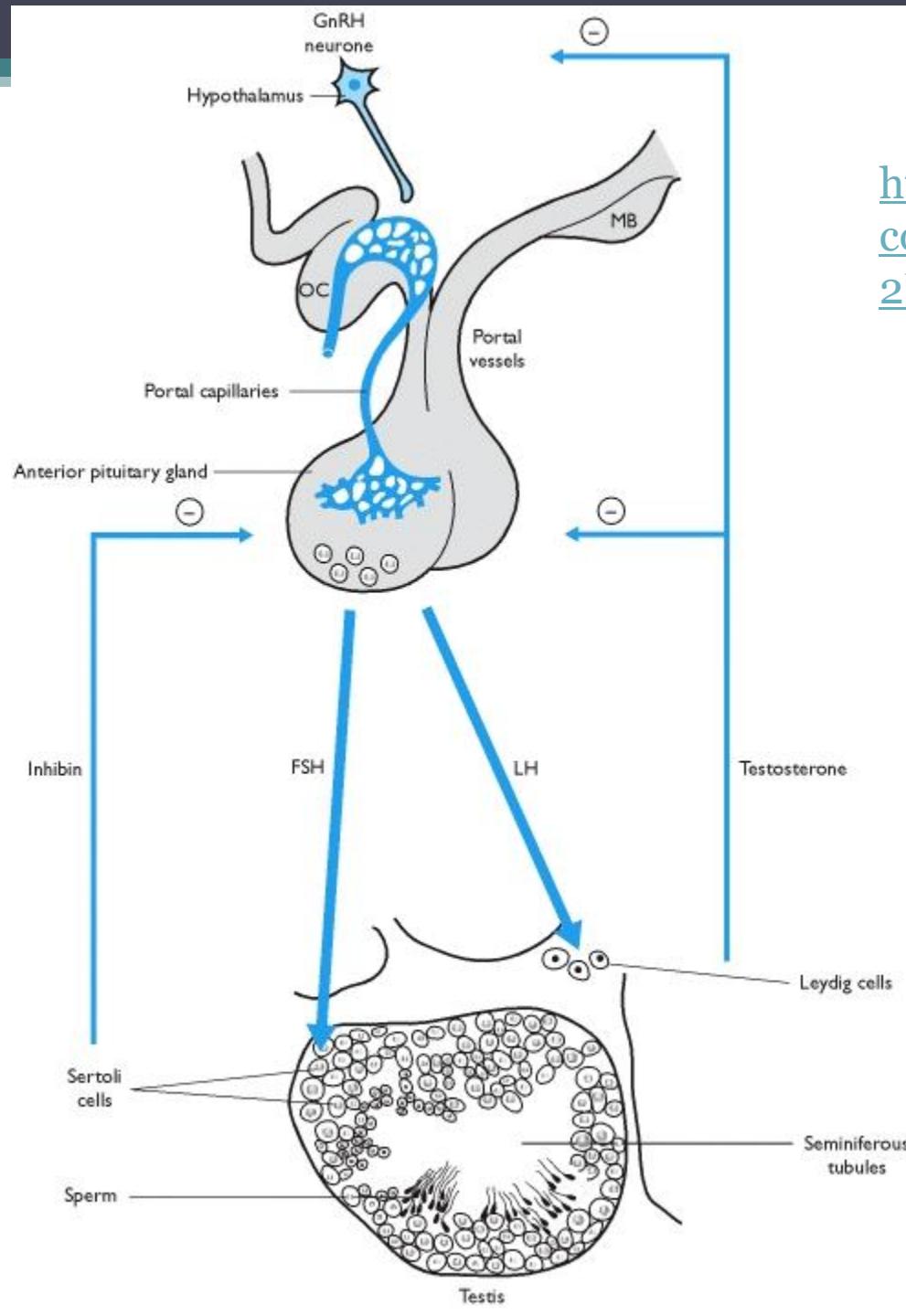
Sperm cell

SPERMATOGENESIS

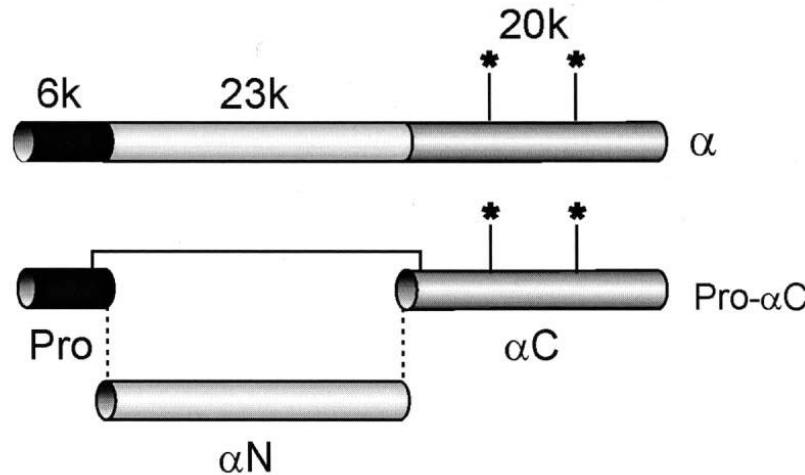




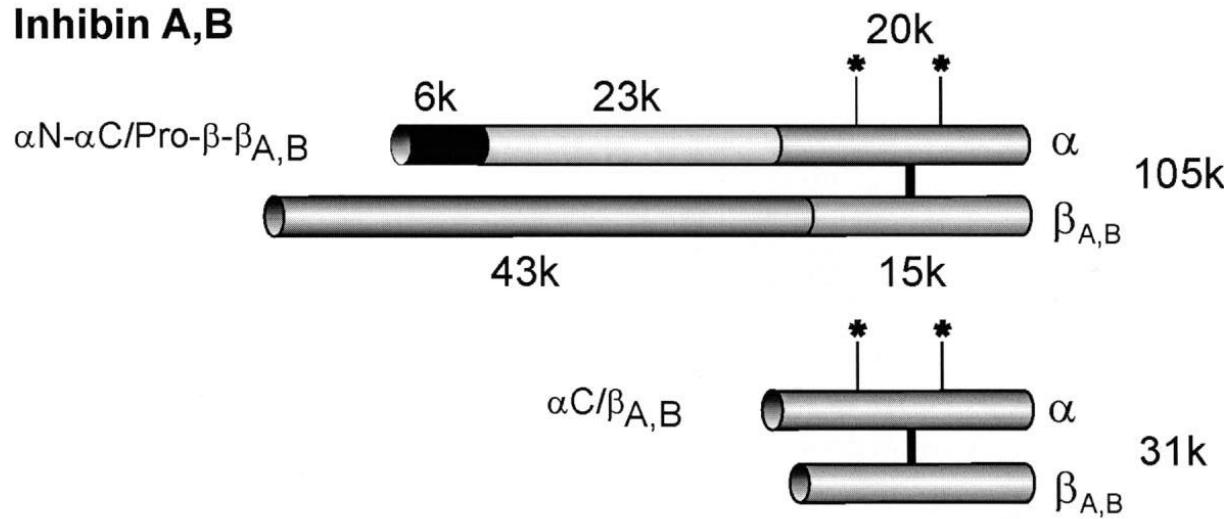
<https://www.youtube.com/watch?v=djqqao2Uebo>



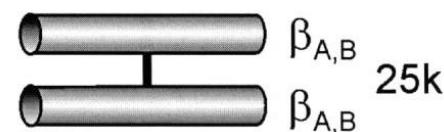
Inhibin α Subunit

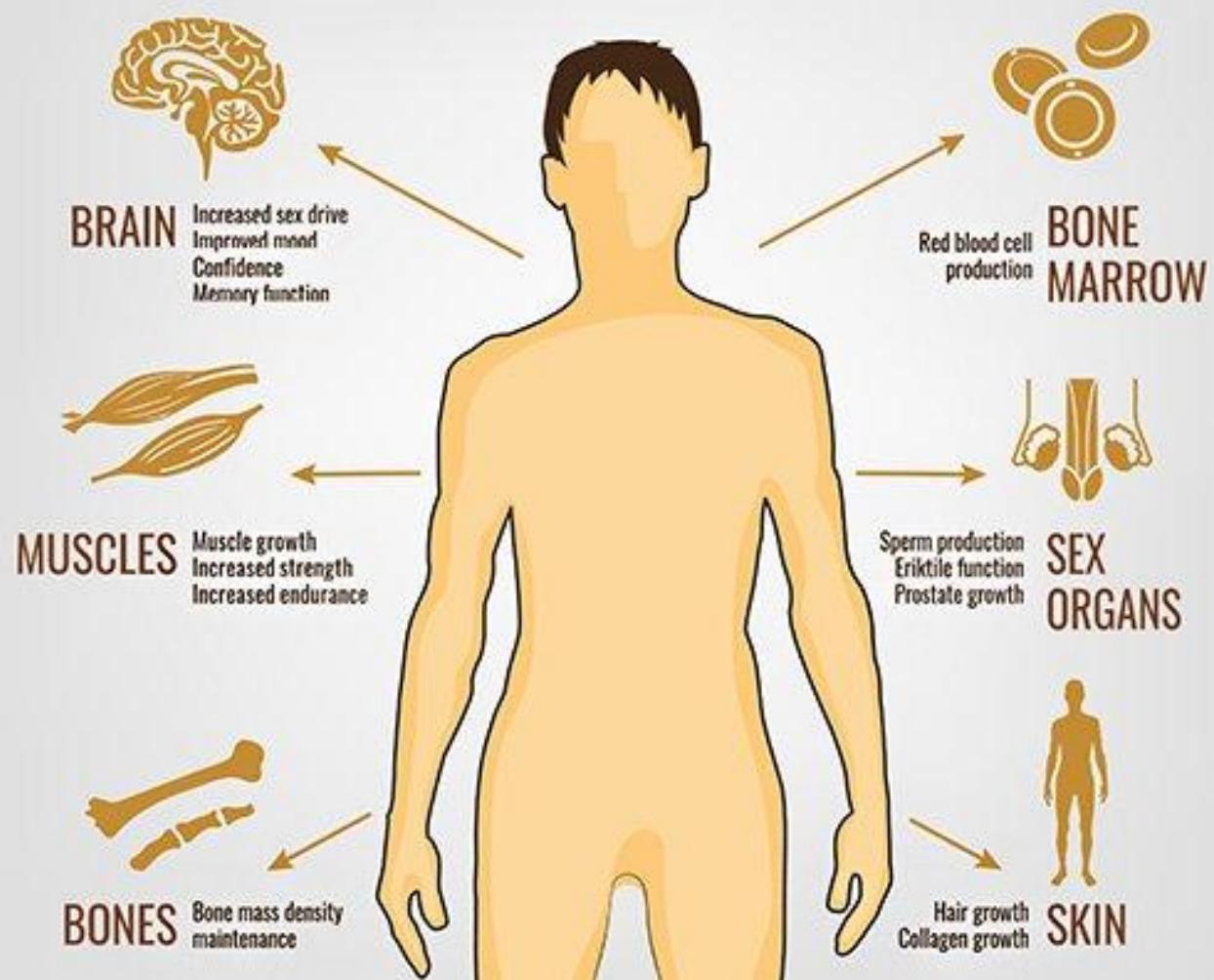


Inhibin A,B

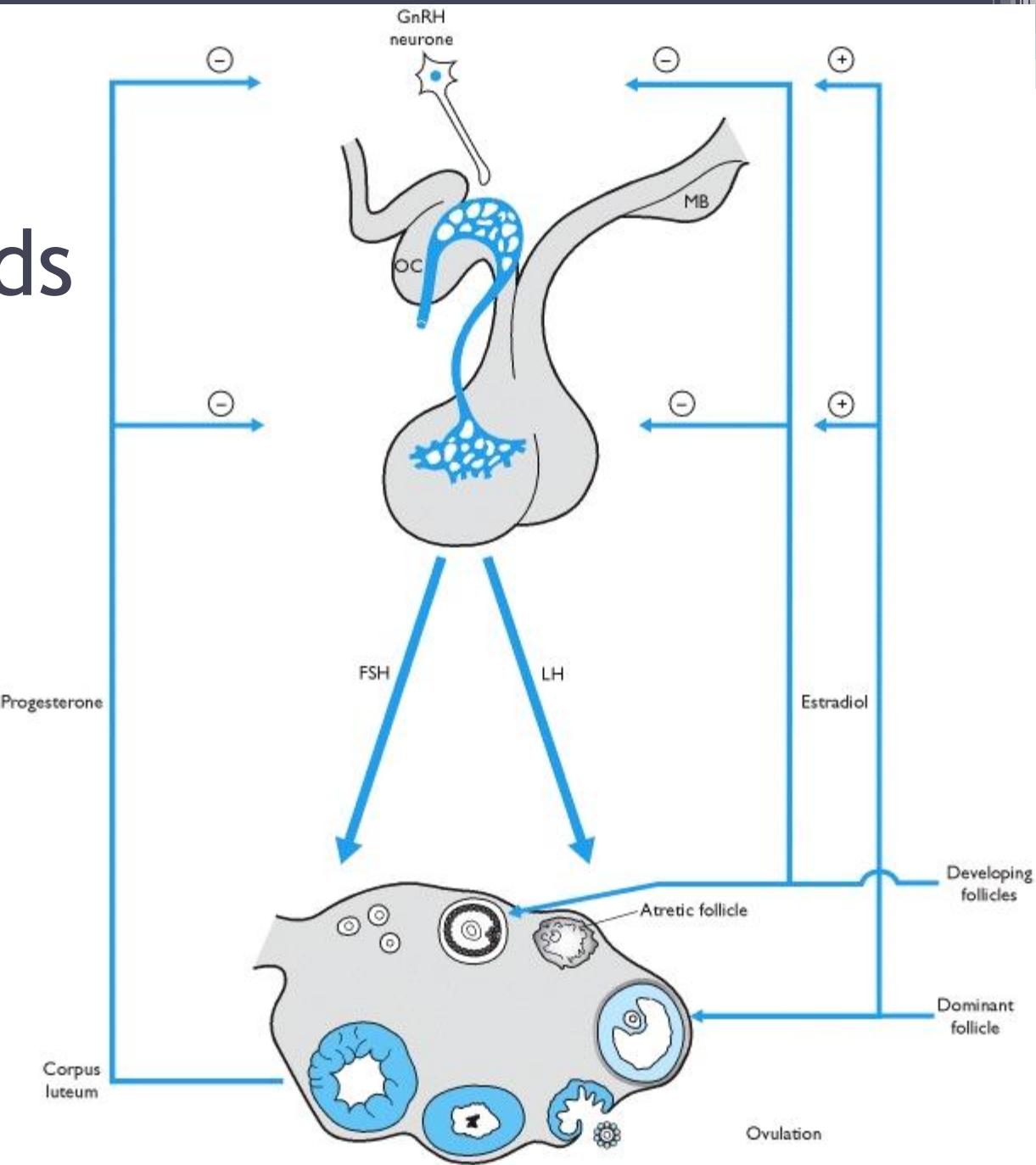


Activin A, AB and B



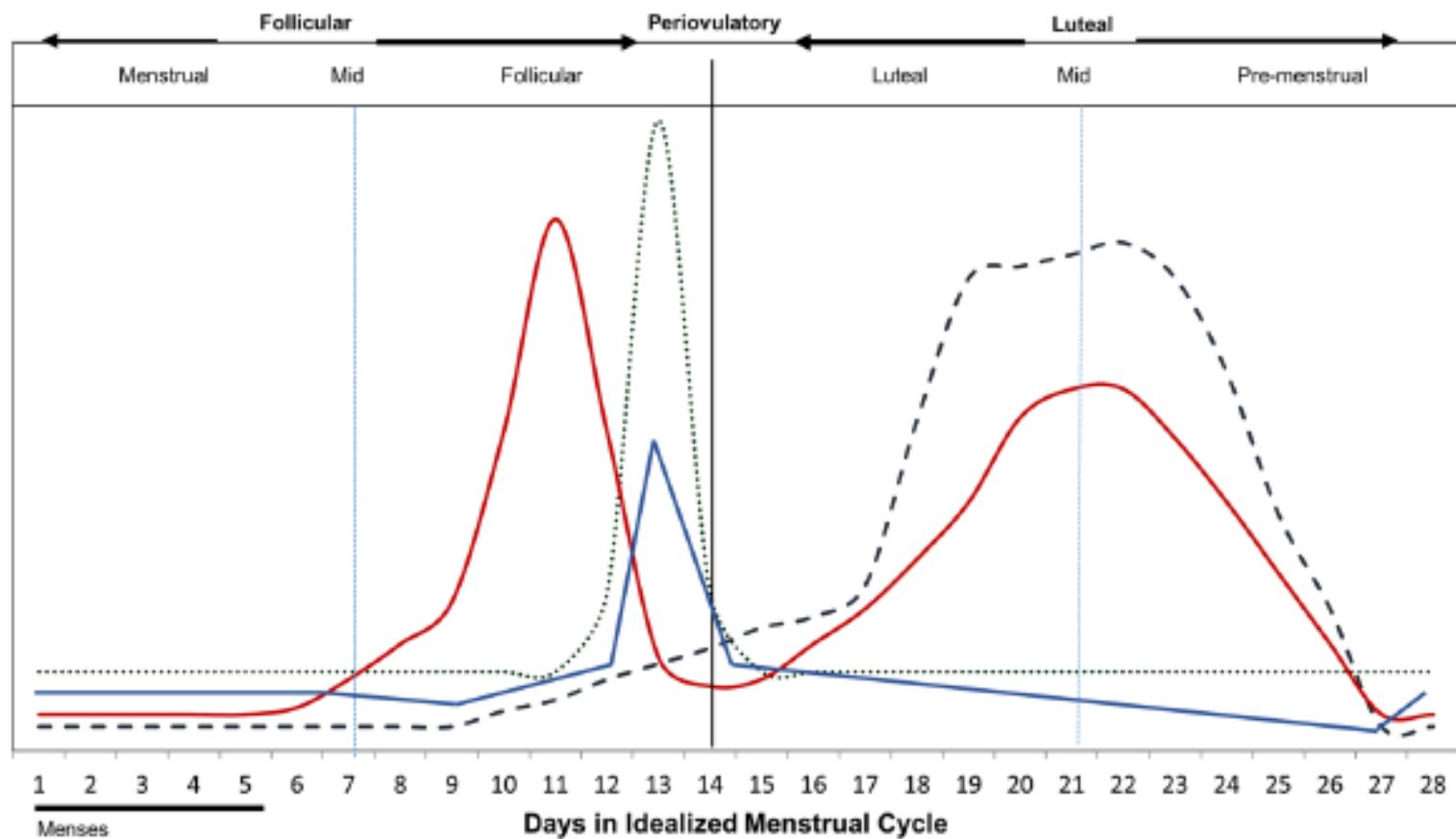


Female gonads

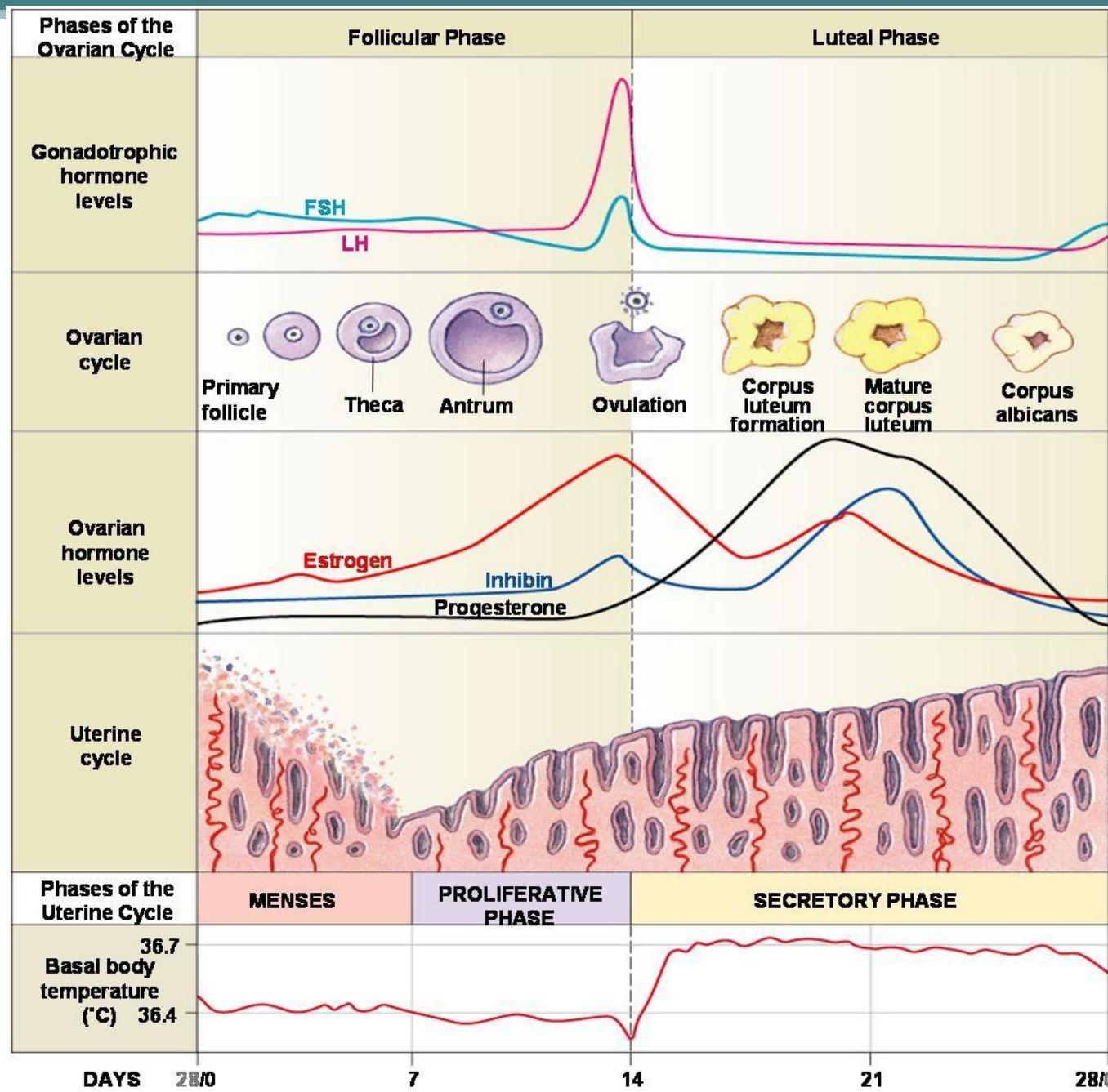


Menstrual cycle

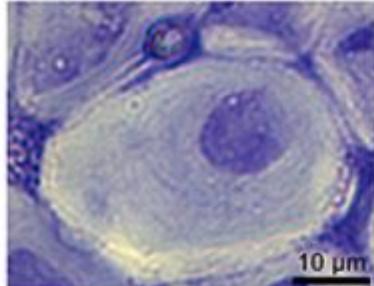
- length of menstrual cycle: 21 to 37 days = time between the 1st day of one period and the 1st day of the next period
- *Menorrhea* - 2 to 7 days
- *Menarche* - 10 - 15 years of age
- *Menopause* - 45 - 55 years of age
- Period stop during pregnancy and breastfeading



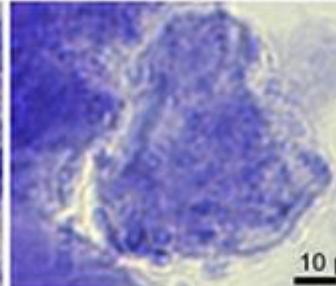
— — — Progesterone (ng/mL) Lutenizing Hormone (mU/mL) — — Estradiol (ng/mL) — — Follicular Stimulating Hormone (mU/mL)



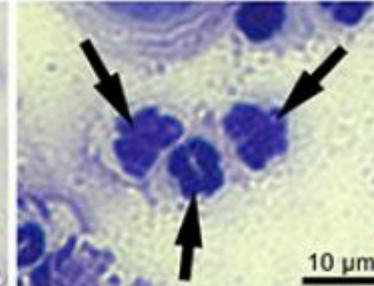
A Nucleated Epithelial Cell



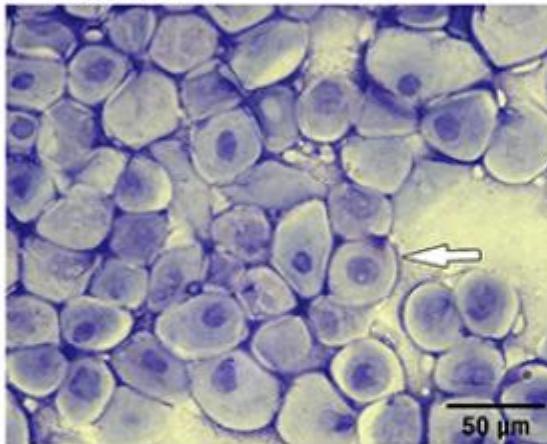
B Cornified Epithelial Cell



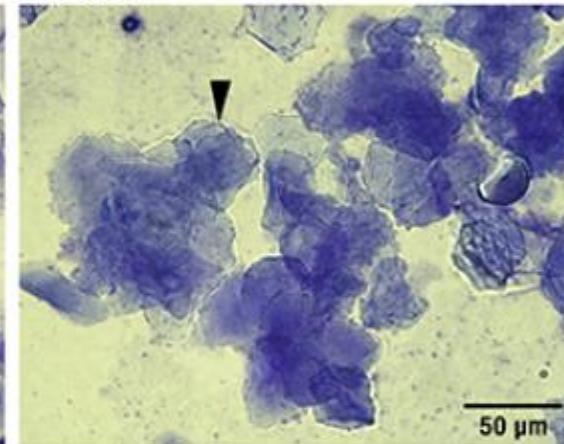
C Leukocytes



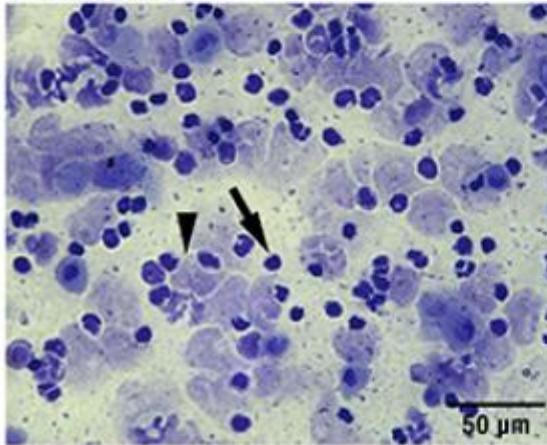
D Proestrus



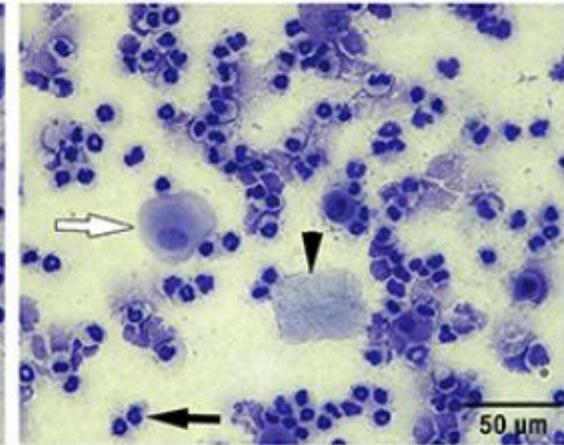
E Estrus

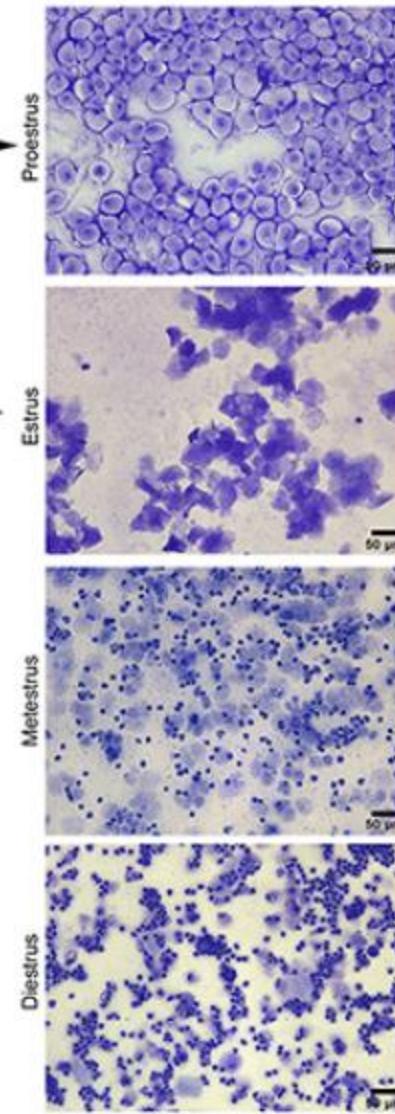
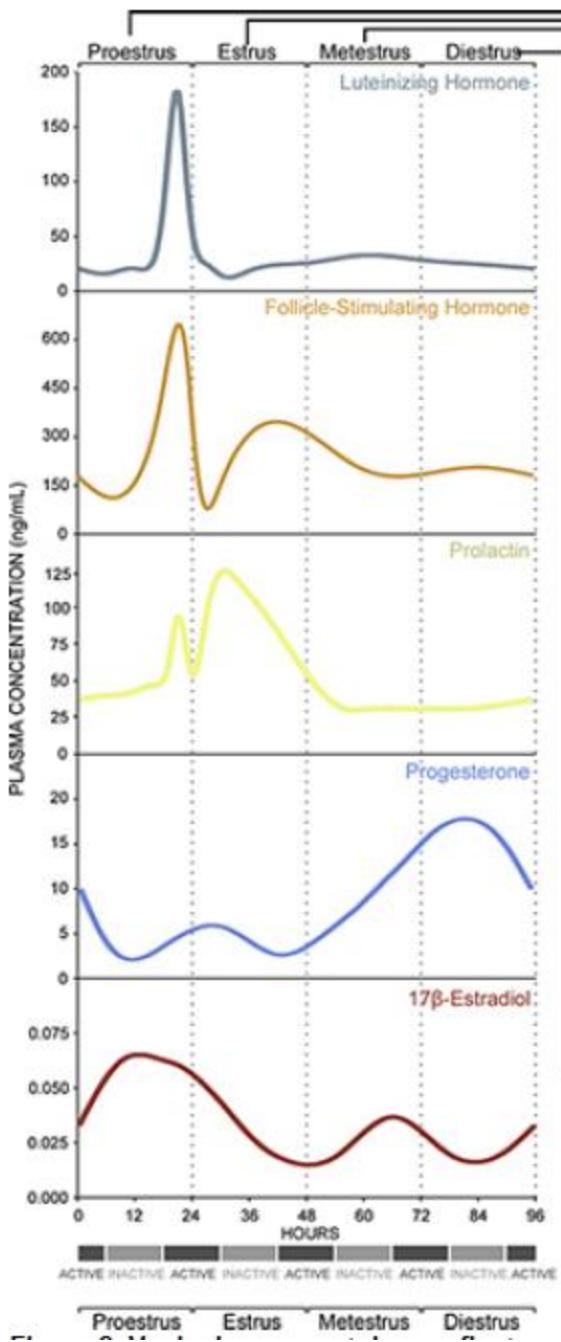


F Metestrus

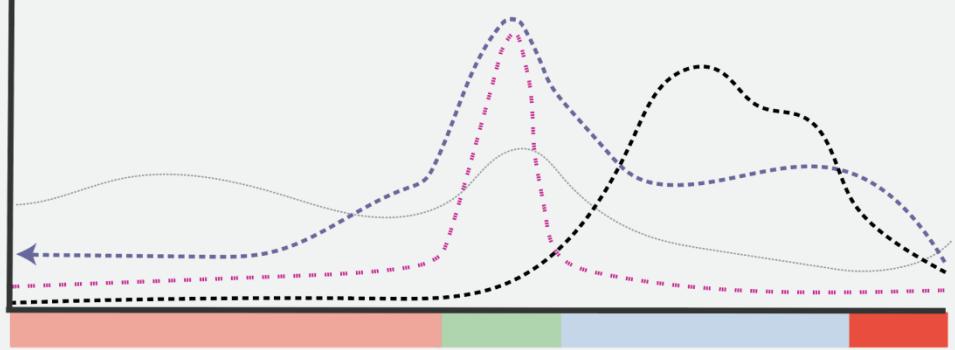


G Diestrus

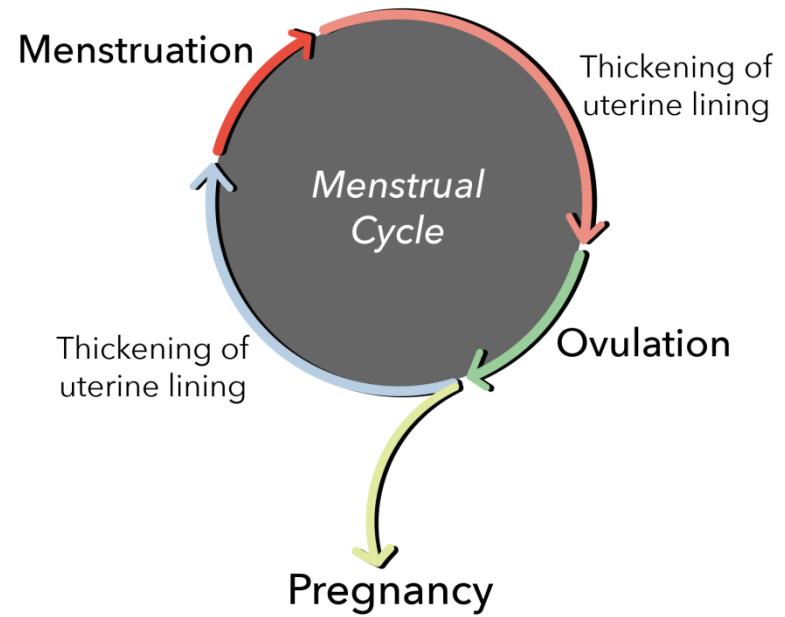
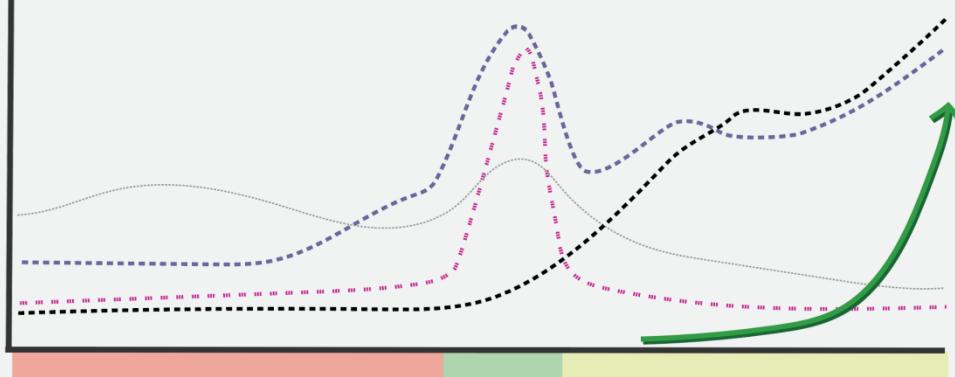




Hormone Changes during Menstrual Cycle



Hormone Changes upon Pregnancy

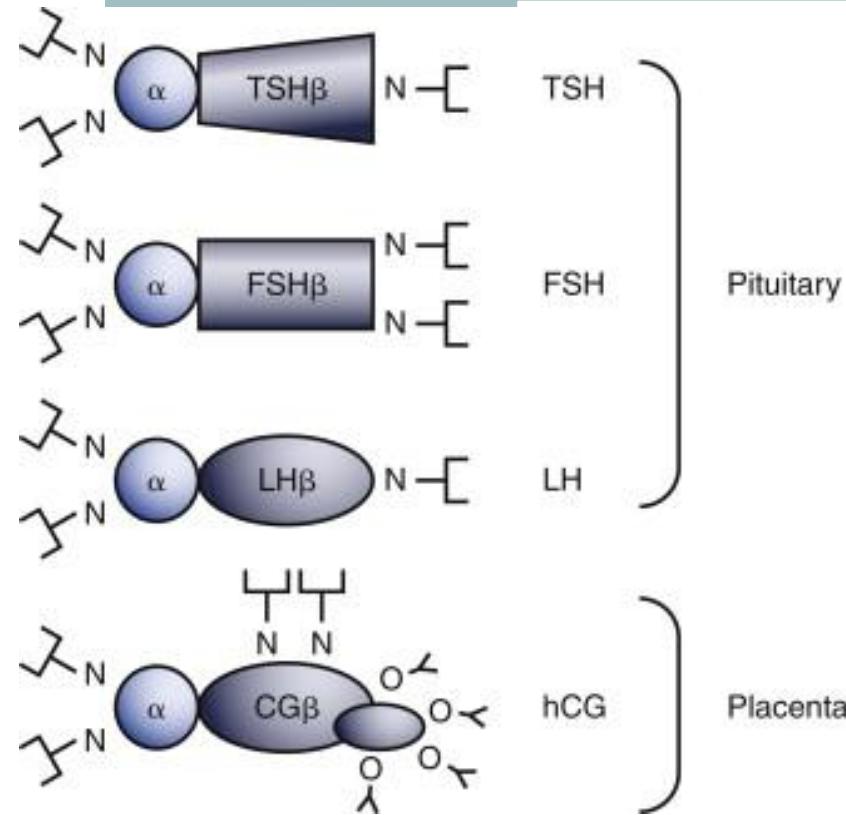


- Lutenizing Hormone
- Follicle Stimulating Hormone
- ... Estrogen
- ... Progesterone
- hCG

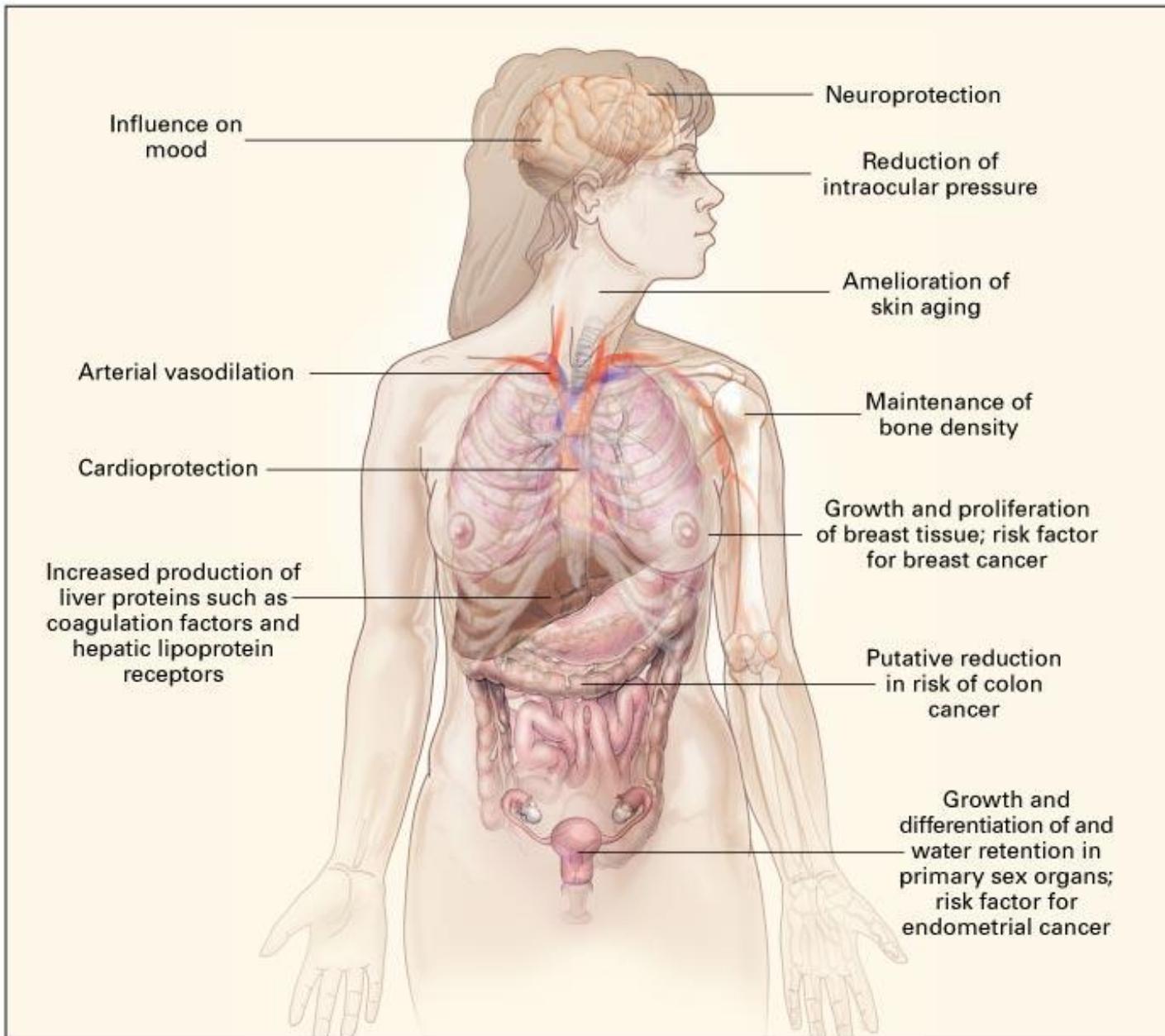


hCG

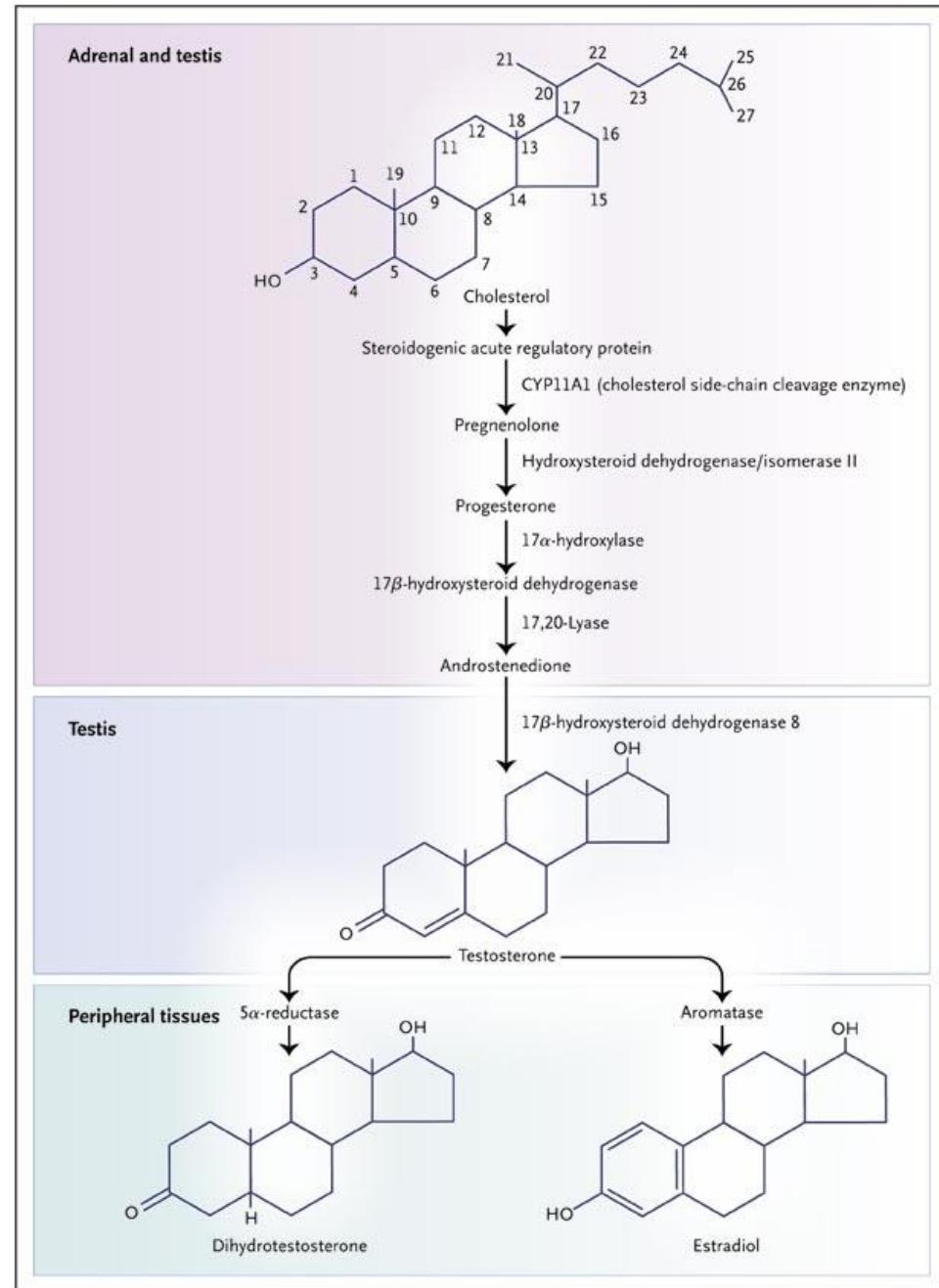
- human chorionic gonadotropin
- syncytiotrophoblast
- first hormonal message
- LH agonist
- stimulates progesterone secretion
- glycoprotein
- α subunit = pituitary gonadotropin hormones
- maternal concentration and glycan structure change all along pregnancy



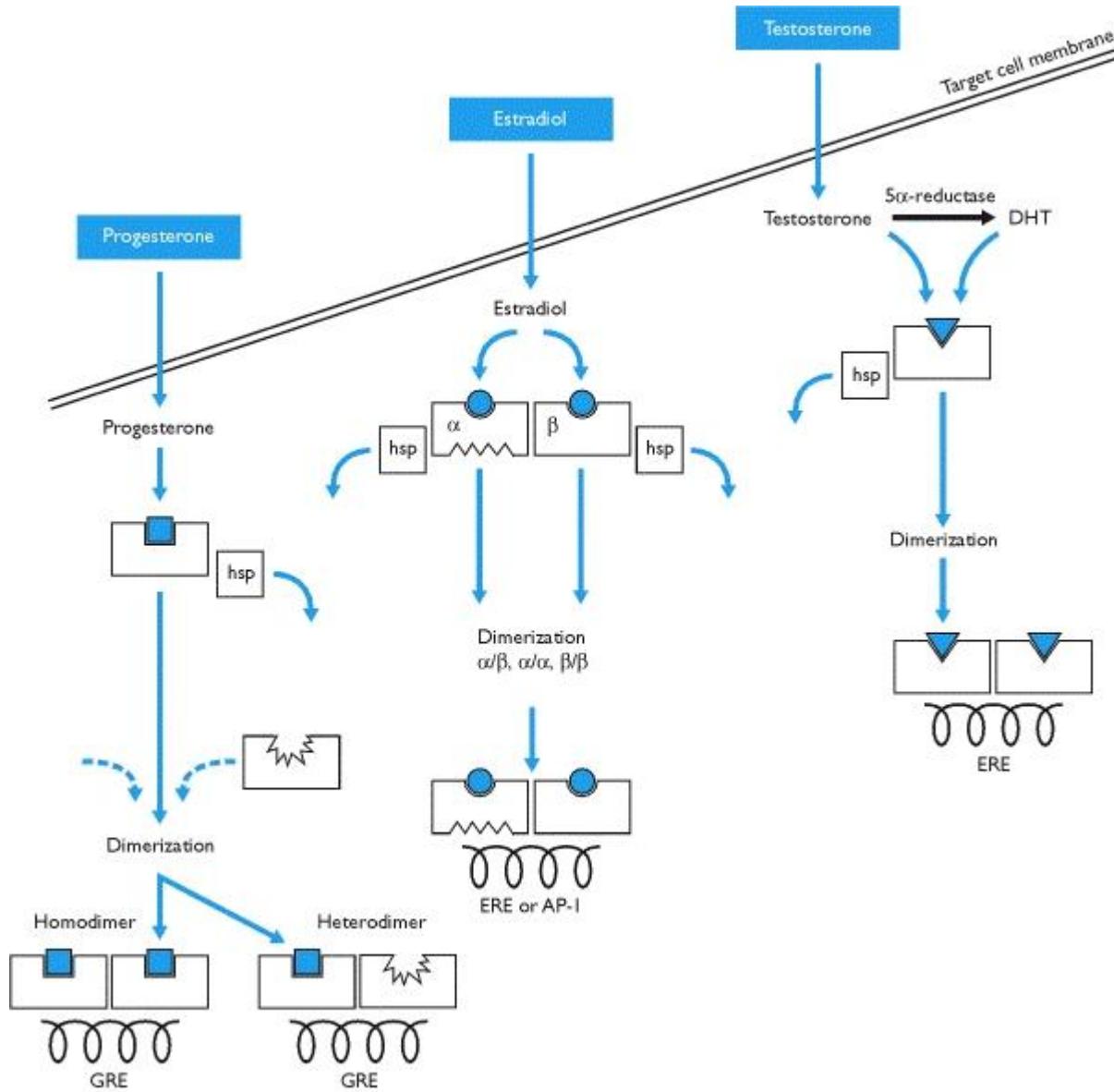
	Estrogen	Progesterone
Actions	Secondary sexual characters: Breast growth, ducts and stroma, Accumulation of fats, pubic/axillary feminine body contour, acne	Cervix: converts watery to viscid scanty and cellular secretions to favour sperm motility
	Metabolic effects: anabolic, ↓ Resorption, ↑calcium absorption, ↑bone remodeling, ↑vit-D3	Metabolism: oral contraceptive impairs glucose tolerance
	↑salt and water, ↑Blood pressure, ↑ glucose, LDL ↑ HDL&TG	Vagina: pregnancy changes , leucocyte infiltration Breast: proliferation of acni duct CNS: Sedative effect Temp: 0.5C ↑ luteal phase
	↑ Coagulability (II,VII, IX, X)	Stimulate respiration
	↑Fibrinolytic activity	↑LDL/ ↓HDL
Antagonist	Tamoxifen Clomiphene	Mifepristone

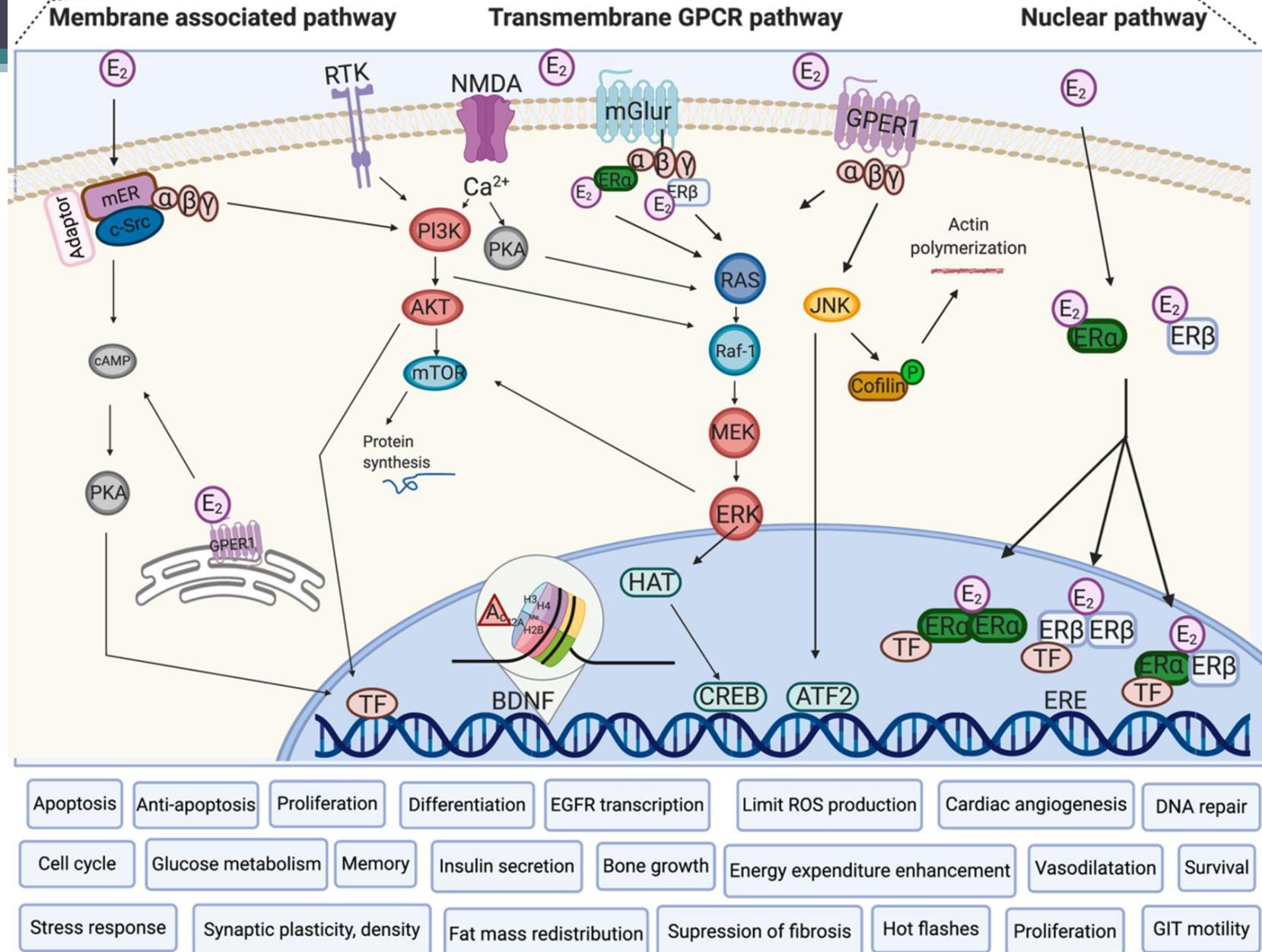


		Testis	Adrenal	Peripheral conversion
Male				
Testosterone	95	<1	<5	
5 α -DHT	20	<1	80	
Androstenedione	20	<1	90	
DHEA	2	<1	98	
DHEA-S	<10	90	-	
Female				
	Ovary	Adrenal		Peripheral conversion
Testosterone	5–25	5–25	50–70	
5 α -DHT	-	-	100	
Androstenedione	45–60	30–45	10	
DHEA	20	80	-	
DHEA-S	<5	>95	-	



Mechanism of action





Pillerová M, Borbelyová V, Hodosy J, Riljak V, Renczés E, Frick KM, Tóthová L. On the role of sex steroids in biological functions by classical and non-classical pathways. An update. Front Neuroendocrinol. 2021 Jul;62:100926.

Pathology - females

- Hypogonadism
 - Primary (peripheral) – ↑ LH, FSH (hypergonadotropic female hypogonadism)
 - Congenital: Turner's syndrome (45, Xo), ovarian agenesis or dysgenesis, enzymopathy
 - Acquired: inflammation, cysts, ovariectomy
 - Secondary (central) - ↓ LH, FSH (hypogonadotropic female hypogonadism)
 - Organic lesions: tumors, ischaemia, aneurysm, trauma
 - Functional: psychoemotional stress (psychogenic amenorrhea), weight loss associated with dieting or malnutrition, rigorous exercises, anorexia nervosa

Turner's syndrome (45, X0)

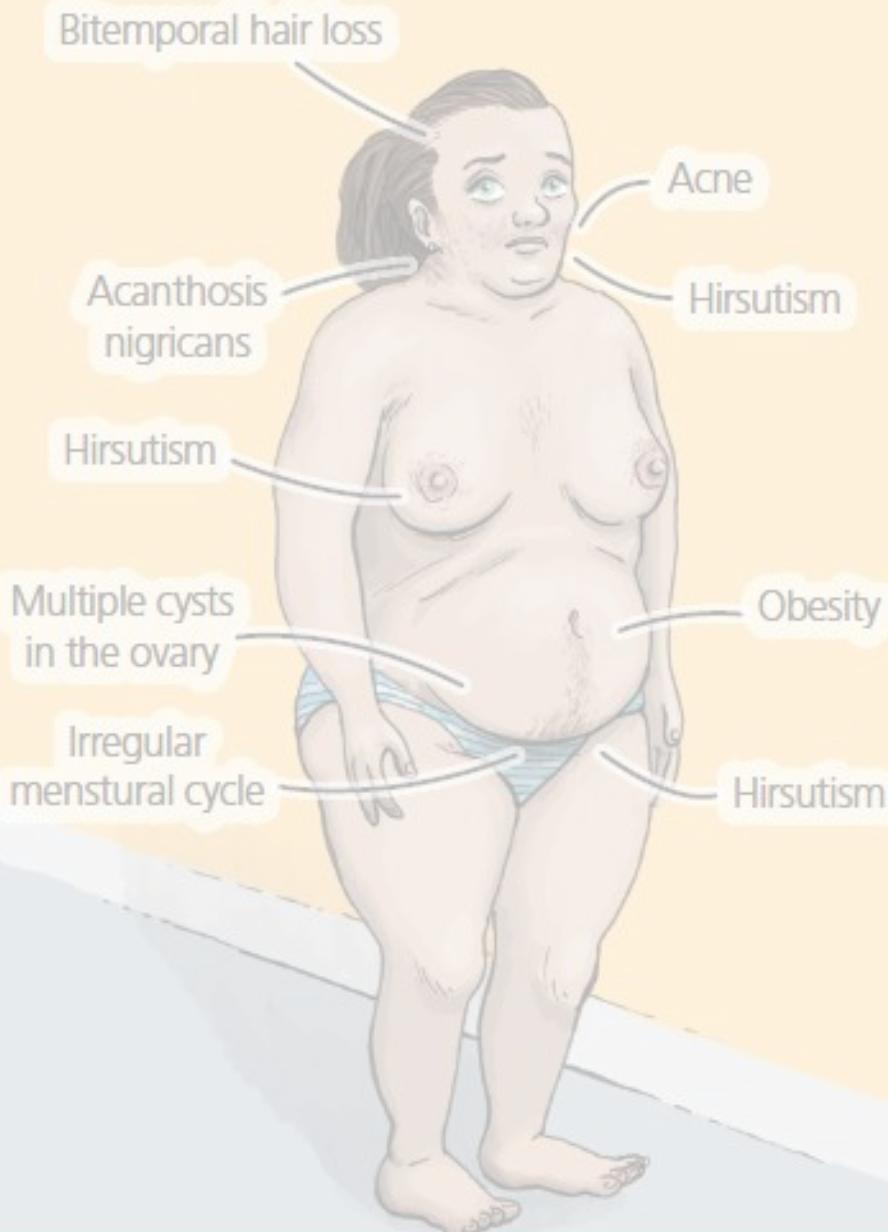
- ↓ E → ↑ gonadotropins
- disorder of sexual maturation
- **Signs and symptoms:**
 - short stature (max 150 cm)
 - genital ducts and external genitalia - female phenotype but immature, infantile
 - no breast development
 - menstruation is absent (primary amenorrhea)
 - multiple congenital anomalies: short and broad neck, redundant skin folds on the back of the neck (pterygium colli), micrognathia (shortened upper jaw), prominent, low-set, rotated or deformed ears or both, a fish-like mouth, a narrow, high arched palate (Gothic palate), a square shield-like chest with widely spaced nipples, increased number of pigmented nevi

Signs and symptoms

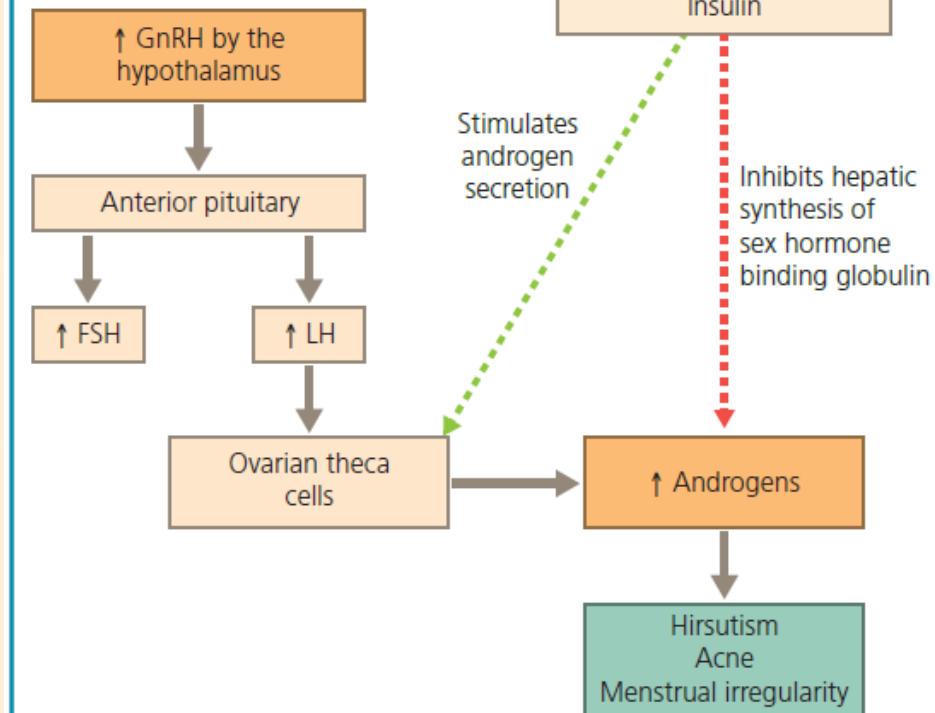
- prior to puberty onset
 - thelarche, pubarche, adrenarche, and menarche are usually absent
 - puberty does not appear spontaneously
 - external and internal genitalia remain infantile
- after puberty
 - amenorea, infertility
 - epiphyseal plates remain open → disproportional growth (**eunuchoidal habitus**)

- Hypergonadism –
 - Primary: ↓ LH, FSH (hypogonadotropic female hypergonadism)
 - Ovarian tumors - feminizing/ virilizing
 - premature sexual maturation
 - menometrorrhagia
 - amenoreia
 - mastodynia
 - Secondary: ↑ LH, FSH (hypergonadotropic female hypergonadism)
 - Polycystic ovarian syndrome

Polycystic ovary syndrome



Polycystic ovary syndrome



Menstrual disorders

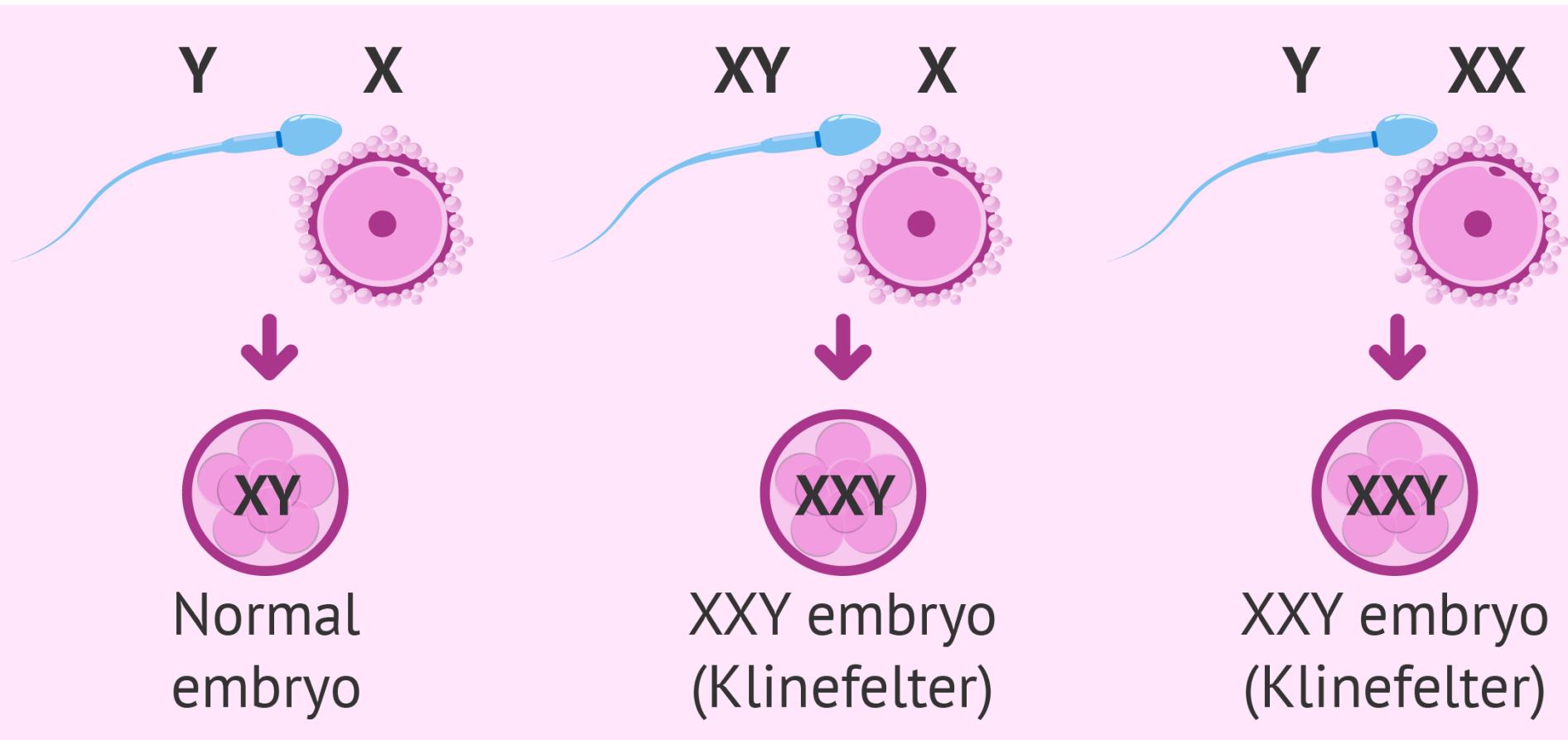
- *Dysmenorrhoea*
- *Menorrhagia*
- *Metrorrhagia*
- *Menometrorrhagia*
- *Amenorrhea*
- *Oligomenorrhea*
- *Polymenorrhea*
- *Hypomenorrhea*
- *Hypermenorrhea*
- *Premenstrual syndrome*

Pathology - males

- Hypogonadism
 - Primary (peripheral) - hypergonadotropic male hypogonadism (\uparrow LH, FSH, \downarrow testosterone)
 - Congenital - Klinefelter's syndrome (47, XXY)
 - Acquired: viral, autoimmune orchitis, antineoplastic and chemotherapeutic drugs, radiotherapy, trauma, castration
 - Secondary (central) - hypogonadotropic male hypogonadism (\downarrow LH, FSH \rightarrow \downarrow testosterone)
 - Causes: organic lesion in hypothalamic-pituitary area, various inborn syndromes (eg. Kallman), hyperprolactinemia, panhypopituitarism

Klinefelter's syndrome (47, XXY)

- cause: gonosomal anomaly
- trisomy XXY
- karyotype : 47,XXY
- nondisjunction of the chromosomes during the meiotic divisions in the course of gametogenesis in one of the parents (40% father in spermatogenesis, 60% mother during oogenesis)



- manifestation: at the time of puberty - FSH is physiologically increased
- dysgenetically changed germinal epithelium of seminiferous tubules of the testes → progressive fibrotization
- histological changes in Leydig cells, but their number is normal or more often increased
- ↓ testosterone (primary male hypogonadism) → ↑ LH by feedback mechanism (hypergonadotropic male hypogonadism)
- relatively ↑ estrogens in plasma → feminization

Causes of male hypogonadism

Primary hypogonadism	Secondary hypogonadism
Haemochromatosis	Haemochromatosis
Klinefelter's syndrome	Kallmann's syndrome
Radiation to testes	Radiotherapy involving the pituitary gland and hypothalamus
Certain drugs (e.g. spironolactone and cyclophosphamide)	Certain drugs (e.g. opiates)
Mumps orchitis	Pituitary and hypothalamic tumours
Trauma	Pituitary and hypothalamic surgery
Undescended testes	Congenital hypopituitarism
Autoimmunity	Hyperprolactinaemia
Systemic diseases (e.g. liver failure and renal failure)	Morbid obesity

Clinical features of male hypogonadism

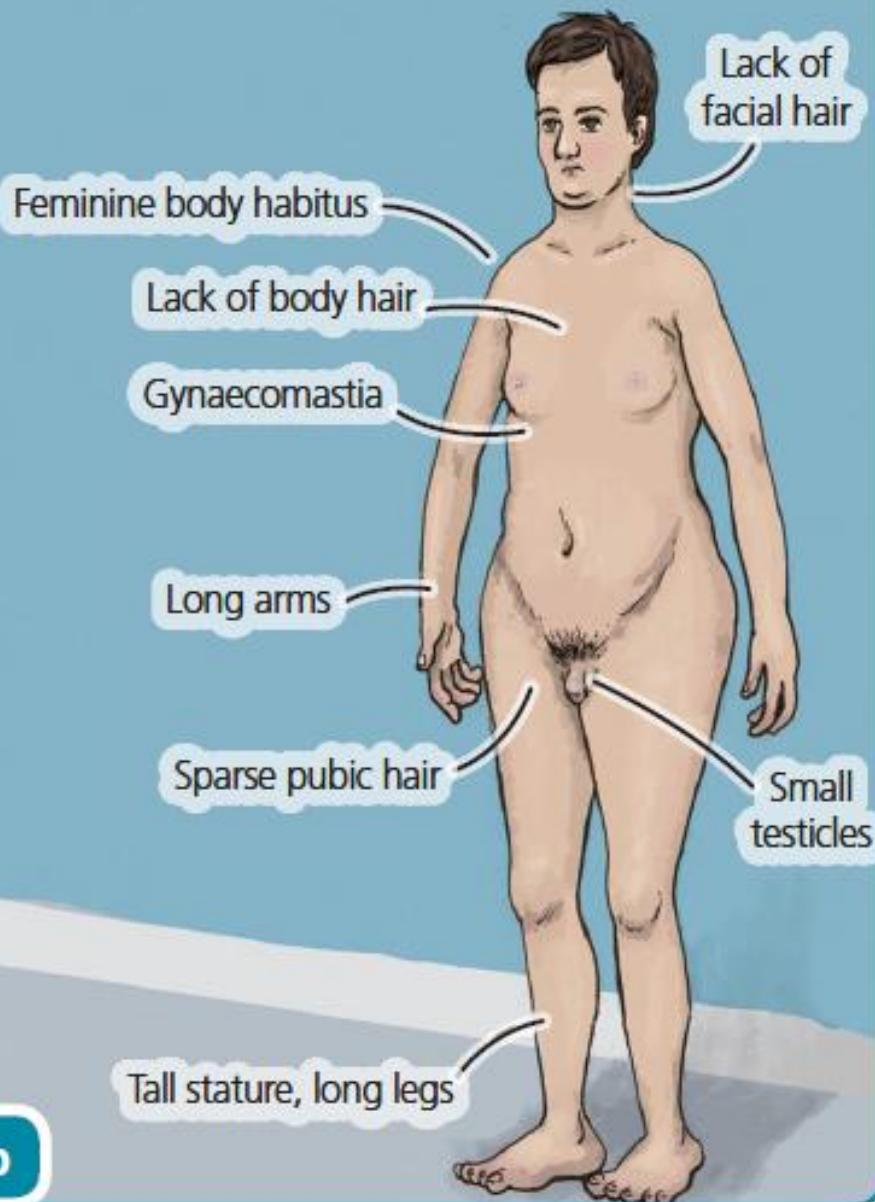
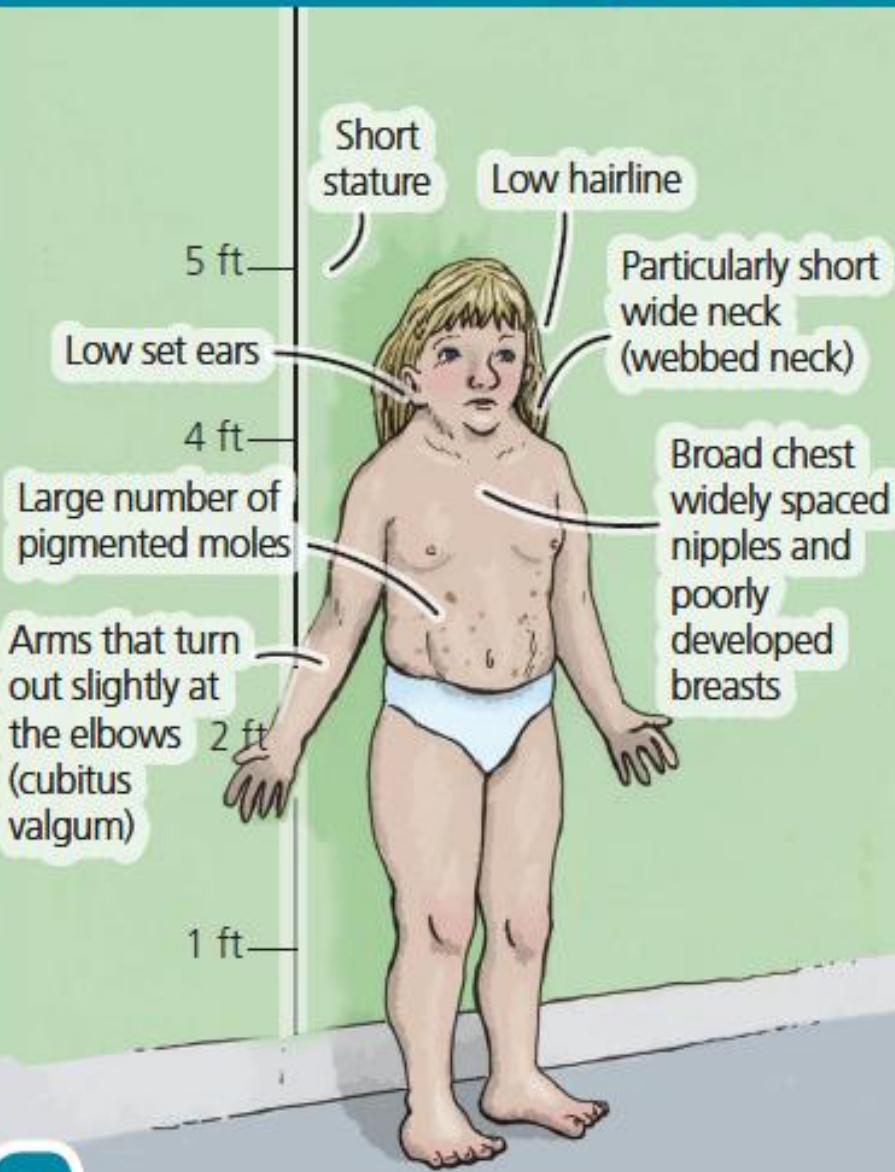
Before puberty	During adulthood
Decreased body and facial hair	Decreased body and facial hair
Gynaecomastia	Gynaecomastia
Small testes and penis	Erectile dysfunction
Poor development of muscles	Decreased muscle mass
Reduced libido	Loss of libido
Unclosed epiphyses	Osteoporosis
Eunuchoid body habitus	Fatigue and lassitude
High-pitched voice	Hot flushes
	Depression and mood changes

- Peripheral hypergonadism – tumors

- hypogonadotropic male hypergonadism:
↑ testosterone/estrogens → ↓ LH, FSH →
↓ testosterone in uninvolved portions of the testes,
azoospermia and decreased size of the contralateral
testis
- age-dependent clinical features
 - Childhood: precocious pseudopuberty: precocious development of genitalia and secondary sexual characteristics, spermatogenesis is absent
 - Adulthood: without any clinical manifestations
- feminization: gynecomastia, thinning of pubic hair,
decrease or even loss of potency, reduced prostate

- Central hypergonadism – tumors
 - hypergonadotropic male hypergonadism:
 \uparrow LH, FSH \rightarrow \uparrow testosterone
 - Causes: organic (tumors) or functional (idiopathic)
 - hypothalamic hamartoma, pineal tumors, other tumors of the pineal region, gonadotropic adenomas of hypophysis
 - less common: hydrocephalus, intracranial aneurysms, encephalitis, sarcoid or tuberculous granulomas of the hypothalamus, arachnoid cysts, or brain abscess
 - Age-dependent clinical features
 - Childhood: true precocious puberty
 - Adulthood: paradoxical low plasma TST, impotency

Turner's syndrome and Klinefelter's syndrome



QUIZ

CONGRATULATIONS!

Lucia Martinkovičová

1. Ktoré tvrdenie **nie** je pravdou?

- A. Tyreoliberín sa produkuje v hypotalame.
- B. Tyreoliberín stimuluje vyplavovanie tyroxínu z adenohypofýzy.
- C. Tyreotropný hormón stimuluje rast štítnej žľazy.

2. Ktoré tvrdenie nie je pravdou pre Gravesovu chorobu?

- A. Je príčinou tyreotoxikózy.
- B. Je autoimúnna choroba.
- C. Je spravádzaná vysokou koncentráciou TSH v krvi.
- D. Jedným z jej hlavných príznakov je strúma.

3. Vápník sa vo vnútri bunky uchováva do

- A. endoplazmatického retikula
- B. mitochondrie

4. Vitamin D sa aktivuje v

- A. pečeni
- B. obličkách
- C. tenkom čreve

5. Glukoneogenéza v pečeni je kortizolom

- A. inhibovaná
- B. stimulovaná

6. Produkcia mineralokortikoidov v nadobličkách je regulovaná predovšetkým s

A. ACTH

B. RAAS

C. CRH

7. Medzi hlavné komponenty metabolického syndrómu nepatrí

- A. Inzulínová resistencia
- B. Dyslipidémia
- C. Centrálna obezita
- D. Nefropátia
- E. Hypertenzia

8. Katecholamíny spôsobujú

A. vazokonstrikciu

B. vazodilatáciu

C. obe

9. Grafitové škrvny sú

- A. znakom hyperadrenokorticizmu
- B. spojené s vysokou produkciou ACTH
- C. spôsobené hypoxiou tkaniva následkom vazokonstrikcie

10. Medzi hlavné príznamy diabetus mellitus nepatrí

- A. únava
- B. anúria
- C. hyperglykémia
- D. strata hmotnosti