المقرر	الفرقة	المحاضرات	نوع المادة العلمية	بيانات التواصل
الهرمونات (لائحة قديمة)	الثالثة	من 6 إلى 9	PDF	01003899211

Effects of Thyroid Hormones on the Cardiovascular System

- Increase heart rate
- Increase force of cardiac contractions
- Increase stroke volume
- Increase Cardiac output
- Up-regulate catecholamine receptors

Effects of Thyroid Hormones on the Respiratory System

- Increase resting respiratory rate
- Increase minute ventilation
- Increase **ventilatory** response to hypercapnia and **hypoxia**

Effects of Thyroid Hormones on the Renal System

- Increase blood flow
- Increase glomerular filtration rate

- **Effects of Thyroid Hormones on Oxygen-Carrying Capacity**

- Increase RBC mass
- Increase oxygen dissociation from hemoglobin

Effects of Thyroid Hormones on Intermediary Metabolism

- Increase glucose absorption from the GI tract
- Increase carbohydrate, lipid and protein turnover
- Down-regulate insulin receptors
- Increase substrate availability

Effects Thyroid Hormones in Growth and Tissue Development

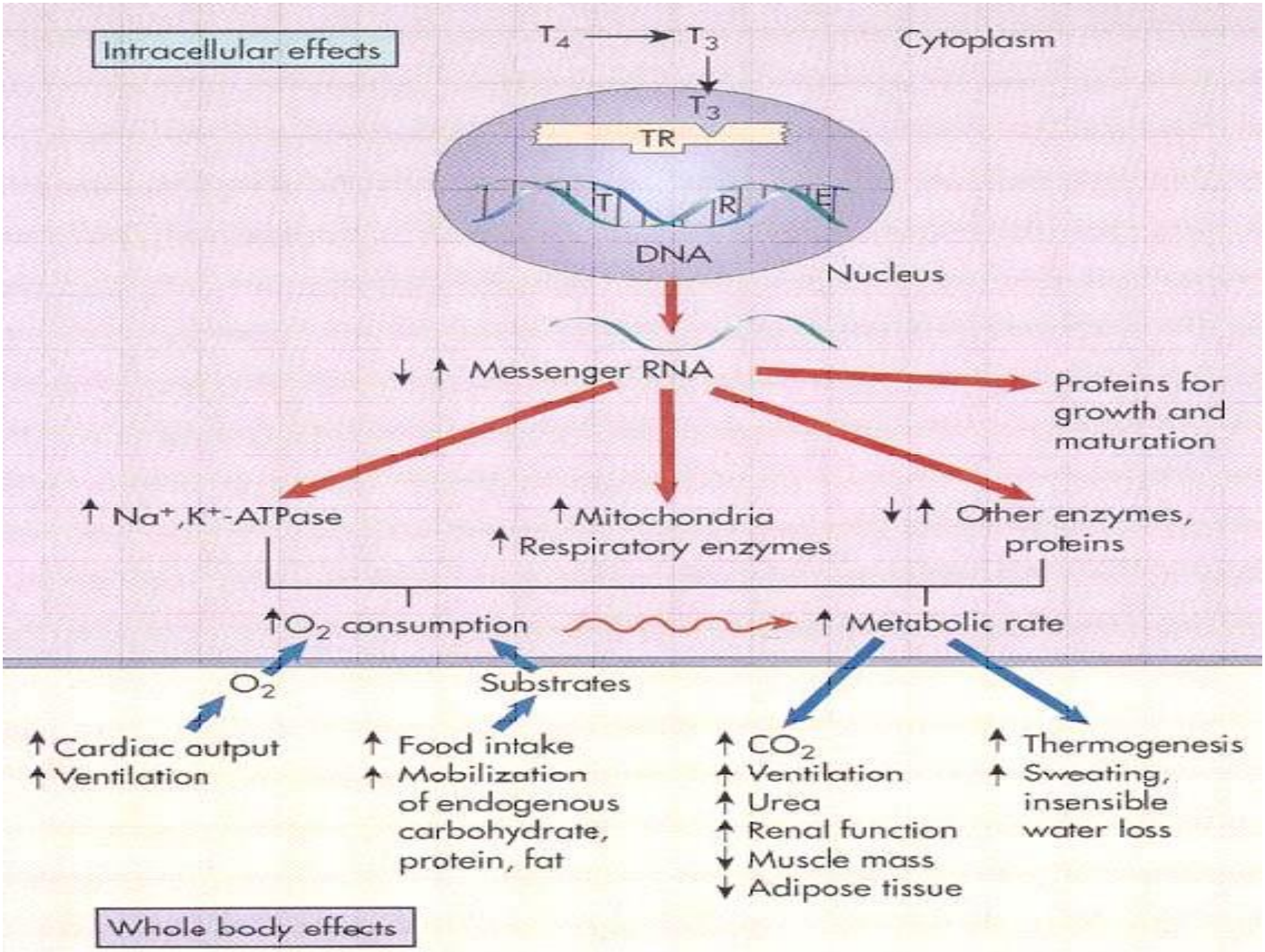
- Increase growth and maturation of bone
- Increase tooth development and eruption
- Increase growth and maturation of epidermis, hair follicles and nails
- Increase rate and force of skeletal muscle contraction
- Inhibits synthesis and increases degradation of mucopolysaccharides in subcutaneous tissue

Effects of Thyroid Hormones on the Nervous System

- Critical for normal CNS neuronal development
- Enhances wakefulness and alertness
- Enhances memory and learning capacity
- Required for normal emotional tone
- Increase speed and amplitude of peripheral nerve reflexes

Effects of Thyroid Hormones on the Reproductive System

- Required for normal follicular development and ovulation in the female
- Required for the normal maintenance of pregnancy
- Required for normal spermatogenesis in the male


Intracellular effects
T_4 → T_3
Cytoplasm
T_3
TR
T
R
E
DNA
Nucleus
↓ ↑ Messenger RNA
Proteins for growth and maturation
↑ Na^+,K^+-ATPase
↑ Mitochondria
↑ Respiratory enzymes
↓ ↑ Other enzymes, proteins
↑ O_2 consumption
↑ Metabolic rate
O_2
Substrates
↑ Cardiac output
↑ Ventilation
↑ Food intake
↑ Mobilization of endogenous carbohydrate, protein, fat
↑ CO_2
↑ Ventilation
↑ Urea
↑ Renal function
↓ Muscle mass
↓ Adipose tissue
↑ Thermogenesis
↑ Sweating, insensible water loss
Whole body effects

Thyroid Hormone Deficiency: Hypothyroidism

- **Early onset** : Delayed/incomplete physical and mental development
- **Later onset (youth)** : Impaired physical growth
- **Adult onset (myxedema)**: Gradual changes occur.

(Tiredness, lethargy, decreased metabolic rate, slowing of mental function and motor activity, cold intolerance, weight gain, goiter, hair loss, dry skin.)

Eventually may result in coma.

Causes Hypothyroidism

Insufficient iodine, Lack of thyroid gland, Lack of hormone receptors, Lack of TH binding globulin….)

How is Hypothyroidism Related to Goiter?

- During iodine deficiency, thyroid hormone production decreases.
- This results in increased TSH release (less negative feedback).
- TSH acts on thyroid, increasing blood flow, and stimulating follicular cells and increasing colloid production.

How is Hypothyroidism Related to Goiter?

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Midwest – the *Goiter Belt*

- If goiter is due to decreased I, then thyroid gland enlarges – called endemic or colloidal goiter.
- Pituitary gland → TSH to stim thyroid gland to produce TH, but the only result is that the follicles accumulate more and more unusable colloid.
- Cells eventually die from overactivity and the gland atrophies.

Thyroid Hormone Excess: Hyperthyroidism

- Emotional symptoms (nervousness, irritability), fatigue, heat intolerance, elevated metabolic rate, weight loss, tachycardia, goiter, muscle wasting, apparent bulging of eyes, may develop congestive heart failure.
- Also due to many causes (excessive TSH release, autoimmune disorders,…)

How is Goiter Related to Hyperthyroidism?

- Due to excessive stimulation by TSH (thyroglobulin production, enlarged follicles…).
- In this case, excessive stimulation of the thyroid gland by TSH DOES result in thyroid hormone secretion, since iodine is available.

Calcitonin (Thyrocalcitonin):-

Structure & functions:- *- It is a peptide hormone secreted by the parafollicular C. cell of the thyroid gland. *- It is involved in the process of calcium regulation. *- It is composed of 32 A.As. (M.wt. 23 Kda). *- It is a calcium lowering hormone (in serum), having metabolic effects opposite to these of para thyroid hormones. *- Calcitonin secretion is stimulated by high plasma ionised calcium. *- It increases the deposition of calcium in bones. (i) - Pituitary (ii)- Thyroid (iii) – Parathyroid hormone:- *- It is a straight-chain polypeptide.

Action:- *- On kidney helping the excretion of phosphate (phosphate diuresis). *- Regulation of calcium & phosphorous levels in the blood. *- On bones, helping the mobilization of calcium from bones.

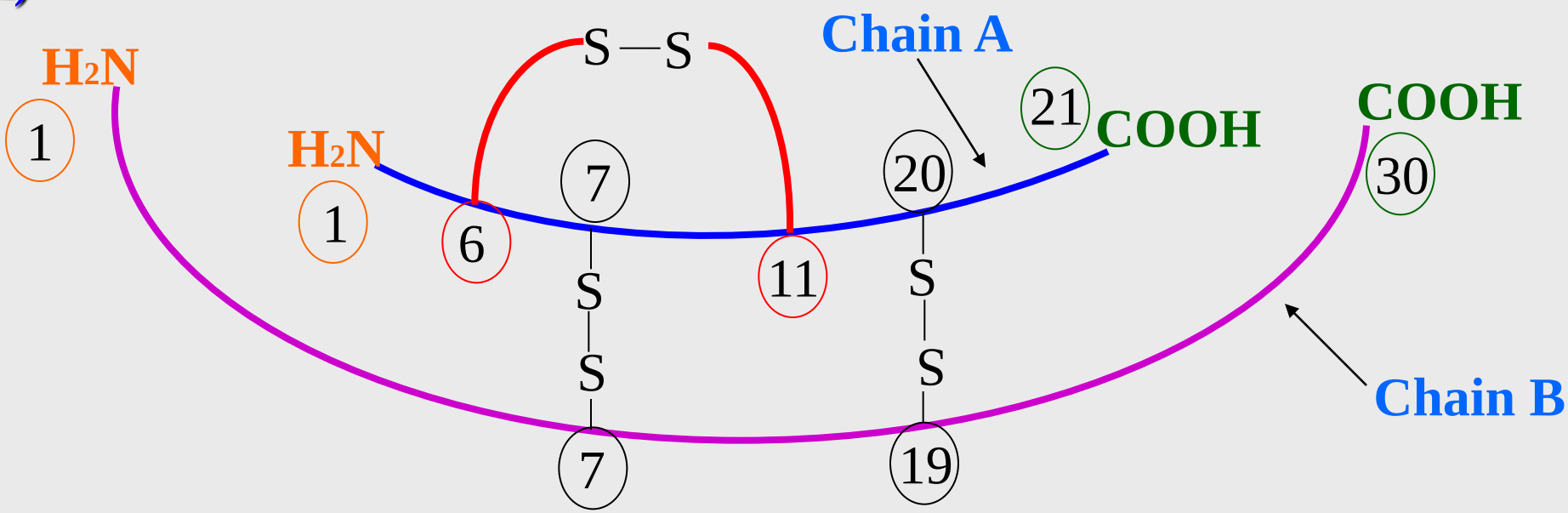
Pancreatic hormones

*- The endocrine functions of the pancreas are located in the islets of langerhans. *- Two hormones are produced by these islets they are (Insulin & glucagon).

a- Insulin

*- It is a protein hormone, that has been isolated from pancreas and prepared in crystalline form. *- Crystalization insulin requires Zn & this appears to be a constituent of stored pancreatic insulin.

*- It M.wt. Is 36 Kda and is composed of Z polypeptide chaine of total 51 A.As. Content. (i) - Chain A which contains 21 A.As. and (ii) – Chain B which contains 30 A.As.



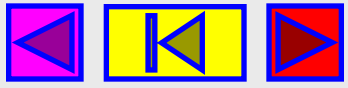
*- The 2 chains are connected by 2 inter-chain disulphide bonds, the first between A.As. no.7 of chain A and A.As. No. 7 of chain B and the second between A.A.20 of chain A & A.A. 19 of chain B.

*- A third diulphide bond (intra) between A.A. 6 & A.A. 11 of chain A is also included. *- In the B-cells, insulin is synthesized as a precursor molecule called pro-insulin.

Biosynthesis:- *- Insulin is synthesized in the polysome (site of synthesis of protein) as pre pro hormone containing 109 A.As.(M.wt.115KDa). *- In the cisternea of the rough endoplasmic reticulum, it lases 23 A.As. giving Proinsulin (86 A.As., M.wt. 90 KDa). *- Proinsulin is formed of B-chain connectiry peptide (C-peptide). *- By the action of proteolytic lysosomal enzymes, proinsulin is converted into Insulin & physiologically inactive C-peptide. *- This free, inactive C-peptide is ultimately secreted in equimolecular ratio with insulin.

Mechanism of action:- *- Insulin receptor is a specific glycoprotein with which insulin bind to exert its action.

*- The receptor is formed of a heterodimer, each unit of the dimer is formed of 2 subunits i.e. α, β subunits. *- The 2 units of the dimer as well as the 2 subunits are linked together by 5-3-bond giving what is called heterotetramer. *- The human receptor precursore is formed from 1382 A.As. (M.wt.190KDa). *- In the rough endoplasmic reticulum, this undergeoes cleavage to give mature human insulin receptors as a single chain peptide.



*- It undegoes extensive & raprd glycosylation in the Glogi region.

*- Removal & sialic acid & gelactose decreases both insulin binding & action.

*- Insulin receptors have $t_{1/2}$ =7- 12 hours, therefor, these receptors are in a continous state of synthesis & degradation.

Adrenal hormones

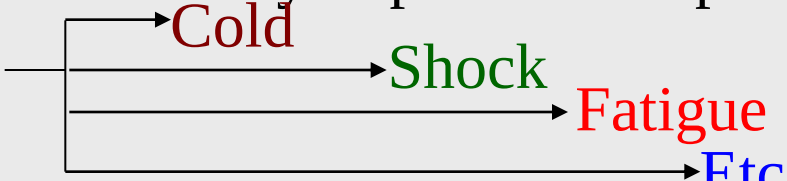
Adrenal invalve adrenal cortex and adrenal medulla.

*- Adrenal medullary hormones:-

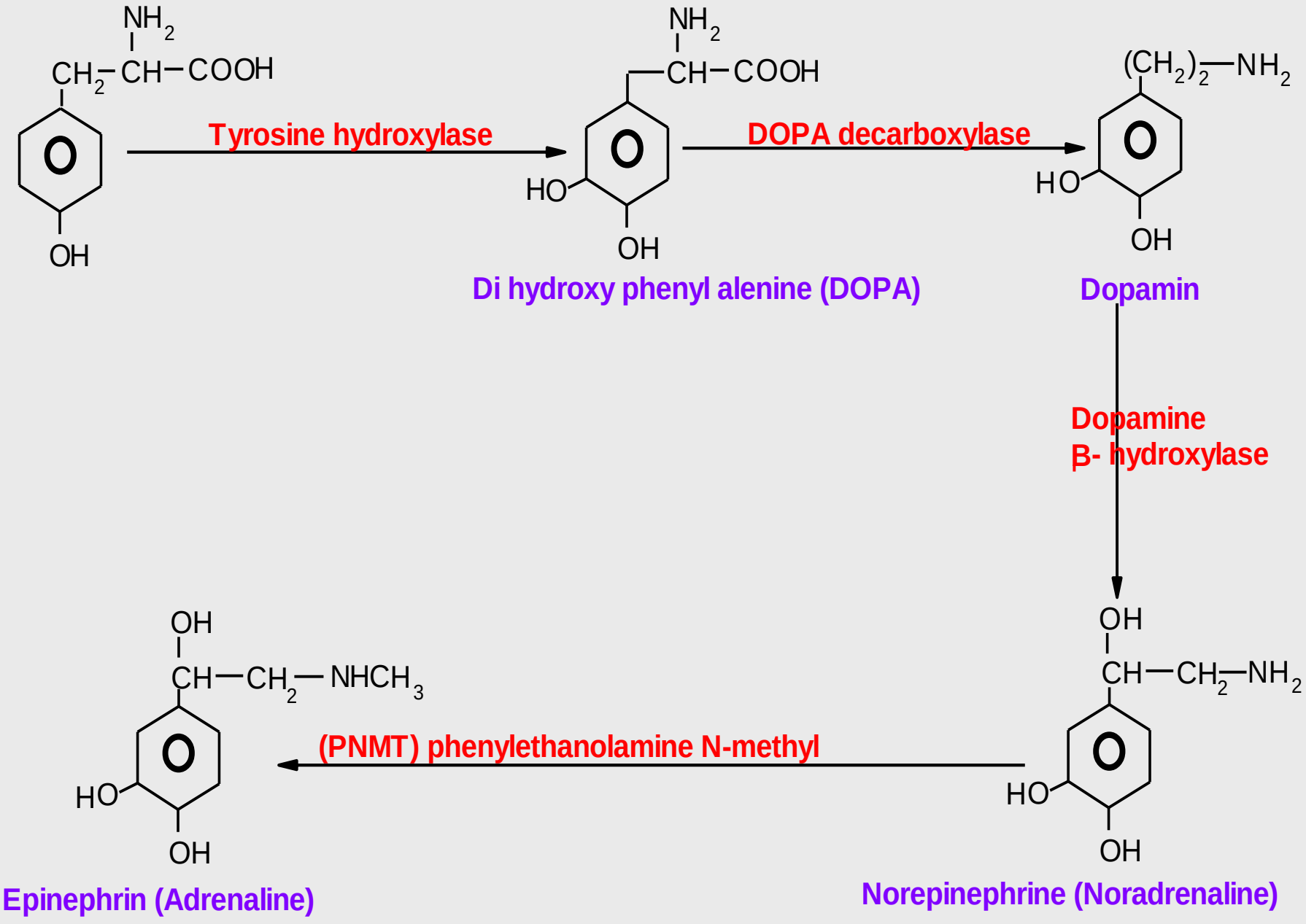
The adrenal medulla secretes ⟶ Catecholamine cepinephrin
Adrenaline and nor epinepherine Noradrenalin.
Catechol amineo

(1)- Biosynthesis:- These hormones acts through 2 major types of receptors:- **(i)-** α-adrenergic receptors:- These are 2 subtypes α_1 – and α_2 – adrenergic receptors. Through these receptors they (?) stimulate cAMP dependent protien kinase and inhibit adenyl cyclase. **(ii)-** β-adrenergic receptors:- These are also β_1- and β_2- receptors catecholamines through these receptors increase cAMP.

(2)- Functions:- *- Epinephrin in general, dublicates the effects of sympathetic nervous system. *- It is necessary to provide a rapid physiologic response to emergencies as



*- **In this respect, it is termed the hormone of fight or flight.**


Tyrosine hydroxylase
DOPA decarboxylase
Di hydroxy phenyl alenine (DOPA)
Dopamin
Dopamine
β- hydroxylase
(PNMT) phenylethanolamine N-methyl
Epinephrin (Adrenaline)
Norepinephrine (Noradrenaline)

(1)- On the cardivascular system:- Both hormones lead to an elevation of blood presures which is more marked in cases of norepinephrine as a result of their actions on heart and blood vessels.

(2)- On the smooth muscles:- Epinephrine causes relaxation of muscles of stomach, intestine, bronchioles & urinary bladder together with contraction of sphincters.

(3)- Metalic effects:- **(a)-** carbohydrates:- ***-** Epinephrine elevate blood glucose level, since it stimulates glycogenolysis in both liver & muscles.

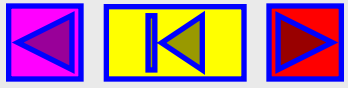
***-** This action is mediated by 3, 5-cAMP. **(b)-** Lipids:- Epinephrine enhances lipolysis, thus, increasing level of free fatty acids in the blood. This is due to stimulation of lipose enzyme, an action which is, also, stimulated by 3, 5-cAMP. **(c)-** Proteins:- Catecholamines have a little catabolic effect on protein as they enhance gluconeogenesis

(d)- Epinephrine has a direct (in hibitory or activatory ??) effect upon insulin release by the pancreas:- It serves as emergency hormone by:-

(i)- Rapidly providing F.As. Which are the fuel of muscles action.

(ii)- Rapidly mobilizing glucose via glycogenolyse.

(iii)- Decreasing insulin secretion, thus, preventing glucose from being taken by peripheral tissue and keeping it for CNS actions.



Catabolism of catecholamines

They are catabolized by 2 enzymes:-

Biosynthesis of adrenal cortex hormones

*- Active acetate (Acetyl Co A) is the precursor of all stroid hormones.

*- At gives chlesterol which is converted to pregnenolone.

*- Pregnenolone (A) either is converted to 17-hydroxy pregnenol (C) which give dehydro epiandroserone (D) or progestrone (B). *- Thus pregnenolone (A) and (C) are converted to a variety of active hormones by spicific **(a)-- oxygences** and **(b)-- dehydrogenases** which require molecular oxygen (in case of (a) and NADP in case of (b).

*- Generally, the results of these enzymatic reactions is the addition of **(i)– Hydroxyl groups** or **(ii)– Ketonic groups** at C_{11}, C_{17} or C_{21} positions. *- In general, C_{21} hydroxylation is necessary for both glucocorticoids & mineralocorticoids.

Catabolism & excretion of stroid hormones

They are catabolized in the liver by:- **(i)-** Reduction of the double bond in the stroid nucleus. **(ii)-** Reduction of the ketonic yp at C_3 .

*- The producted metabolites become conjugated with either:-

(i)- Glucaronic acid (major pathway). **OR** **(ii)-** Sulphated (minor pathway.

*- Most of these metabolites are excreted in bile, however only 20% are excreted in stool. *- The rest (80%) becomes re-absorbed and 70% (of 80%) are excreted in urine and 10% (of 80%) in sweet the remaining 20% of the absorbed 80% are still circulating in the blood.

Metabolic functions

(A)- glucocorticoids

*- The steroids containing OH or C ═ O at C_{11} position and OH at C_{17} have glucocorticoid activities e.g. Corticosterone, hydrocortisone (cortisol), 11-dehydrocorticosterone & cortisone.

*- The most important glucocorticoids are cortisol and corticosterone.

*- They act as steroid hormones by modification of **RNA** and **enzyme synthesis** in the target tissues. *- The are lipophilic hormones ⟶

- ($t_{1/2}$ = ? High (? Days).
- Need carrier.
- Intra or inter cellular receptors.
- Their action is mediated by ??

*- They control carbohydrate, lipid & protein metabolism:-

a- On carbohydrates:- *- They decrease glucose uptake by the inhibition of glucokinase enzyme ⟶ hyperglycomia.

*- They activate inhibit glycolysis. *- They help gluconeogenesis, sine the activities of the enzymes which are involved in amino acids conversion into glucose are increased or decreased (??).

*- The glycogen deposition is increased or decreased (??) (The rate of glycogen formation is not sufficient to control the glucose level).

(In general, the action of glucocorticoids are metabolcally antagonistic to insulin with a consequent rise in blood glucose level i.e. hyperglyccemia is developed).

b- On lipids:- *- Glucocorticoids enhance lipolysis (break down of triglycerides (T.G.) of adipose tissues particulary in the extremeties). Thus, the levels of free fatty acids (FFAs) are increased in the blood.

*- They help gluconeogenesis from the liberated glycerol and of hydrolysis of triglycerides (TG).

c- On protein metabolism:- *- In physiological concentrations, glucocorticoids have anabolic effects. *- Deviation from normality leads to catabolic effects (hypersecretion). *- In the latter case protein synthesis is decreased, wherees protein metabolism is increased.

*- This leads to increased (decreased) excretion of non-protein (NPN) compounds in urine and a state of negative nitrogen balance is developed

d- Other effects of glucocortioids:-

(i)- Anti-inflammatory effects:- As they used in the treatment of collagen diseases as rbeumatoid arthritis.

(ii)- Immune supressive effects:- Cortsol decreases the immune response associated with infection and allergic states.

(iii)- Stress:- Glucocorticoids are elevated several folds in response to a cute stress to reverse the decreased blood presure resulting from emotional or surgical shock.

(iv)- Miscellaneous effects:- *- They increase lung surfactants, consequently, they are used in the treatment of respiratory distress syndrome (RDS) in newly born premature infants. *- They stimulate the secretory functions of gastro-intestinal tract (GIT): e.g. increasing the secretion of HCL, pepsinogen and trypsinogen etc. *- Administration of glucococoticoids, thus, enhances GIT ulceration e.g. (peptic ulcer).

(B)- Mineralocorticoids

*- The most potent mineralocorticoid is aldosterone. *- Its pathway of synthesis needs C_{17} hydroxylation. *- With exception of androgens, all coticoids increase the absorption of Na+ & Cl- by the renal tubules (i.e. reduce Na+ & Cl- excretion). *- However, glucocorticoids e.g. cortisol have the least sodium retaining action while

aldosterone is at least 1000 times as effective as cortisol in this respect.

 # Mineralocorticoids have the following actions:-

(1)- Na+ retaining actions via:- (a)- Reabsorption of Na+ & Cl- is enhanced (or decreased ?) by renal tubules. (b)- Their excretion (?) is also reduced by : (i)- Sweet. & (ii)- GIT.

#

Disturbances of adrenal functions:-

(a)- Disorder of glucocoticoids: ⟶ (Hypofunction)

(i)- Adrenal insufficiency (Adison disease as an example):-

*-It is characterized by: 1- Hypoglycemia. 2- Extreme sensitivity to insulin. 3- Intolerance of stress. 4- severe weakness & nausea. 5- weight loss.

*- This pateint suffer from low blood **pressure** & **decreased glomerular filtration rate** and **ability to excrete H_2O**.

*- Low plasma Na+ (with increased K+), easinophils and lymphocytes.

*- Hyperpegmentation of skin & mucus membranes occurs due to compensatory increase in ACTH (has a similarity of MSH as was previosely reported) secretion (why ???).

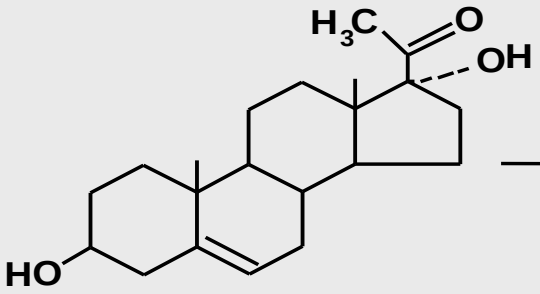
C- Sex hormones

*-The tests&ovaries in addition to their function in providing spermatory or ova synthesize also sex hormones.

(1)- Male sex hormones

*- The princepal male sex hormone is testosterone. *- it is synthesized, mainly, by the leding cells of the tests. *- In addition, androstenedione & dehydroepiandrosterone are also produced. *- The major adrenal androgen, dehydroepiandrosterone is produced by side chain cleavage of 17-hydroxy-pregnenolone.

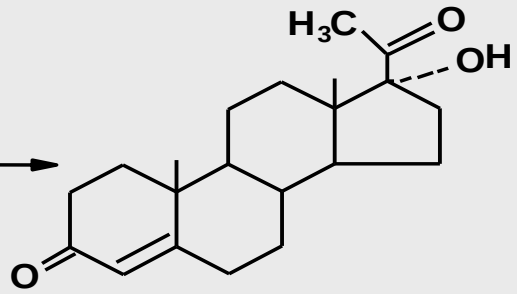
 # - Metabolic actions:- *- **They** have protein anabolic effects, thus producing a state of ? Nitrigen balance. *- **Androgens** promote protein synthesis in male accessoy glands, thus, growth & functions of epididymis, vas deference prostate, seminal vesicles and penis are enhanced. *- **In** general, they are responsible for male secondary sex characters. *- **Excretion** of 17-ketostroids in urine, is in part snsidered to be a reflection of testicular hormonal production. *- **This** tests (measurement of 17-retostroid level) contribute to 1/3 of the total urine ketostroids. *-**In** norml children (male or female) up to 8^{th} year of life **there is a gradual increase in 17-ketostroids excretion with no sex differences.**



17-hydroxy-pregneolone

(i) Dehydrogenase

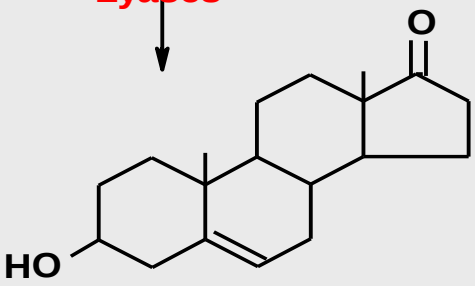
(ii) Isomerase



17-hydroxyprogeste

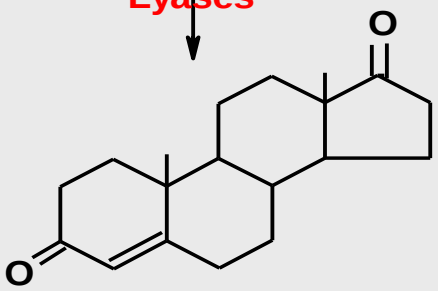
Lyases

Lyases



Dehydroepianderosterone

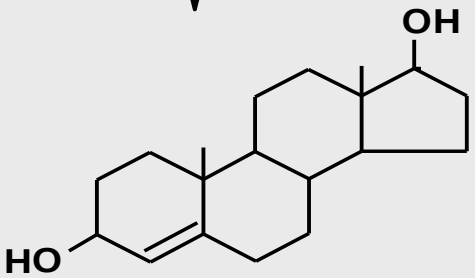
Dehydrogenase



Anderstendione

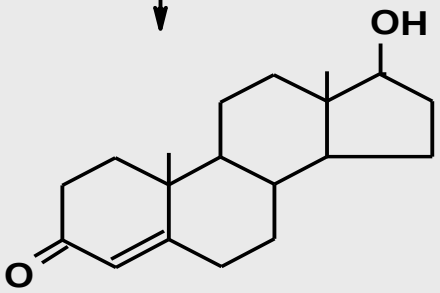
Hydrogenase

Hydrogenase



Androstendiol

Dehydrogenase



Testosterone

*-After puberty, males show higher 17-ketostroids excretion than females.

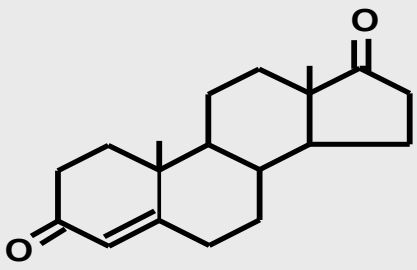
(2)- Female sex hormones

*- The 2 main types of female sex hormones are produced by the ovary.

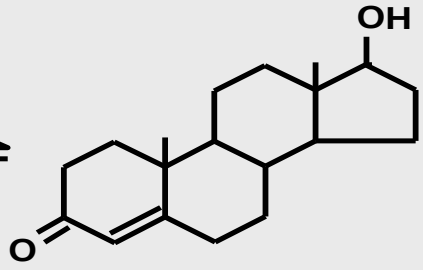
*- These 2 types of hormones include the **folliculer (or strogenic)** hormones which are produced by cells of graffian follicules and **progestronal hormones** (which are derived from corpus leuteum that is formed in the ovary from ruptured follicule). *- Small amounts of adrenal oestrogen are produced from testosteron either from dehydro epiandrosterone or from 17-hydroxyprogestrone.

(i)- Follicular hormones:- *-**They** are C_{18} stroids differing from androgens in lacking methyl group at C_{19}. *- **In** contrast to all other stroids, ring A is aromatic. *- **The** most active hormone in the circulation of all estrogens is oestradoil (E_2). *- **E2 is** a metabolic equilibrium with oestrone (E_1). *- **Estratriol** (E_3) is the principal oestrogen found in urine of **pregnant women**.

*- **E3 is** produced from estron (E_1) by its hydroxylation at C_{16}.



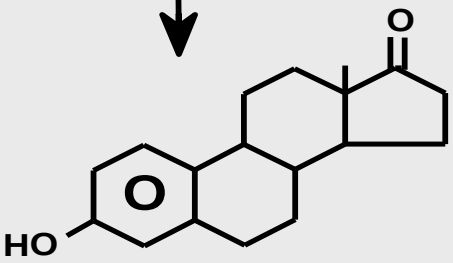
Androstene dione



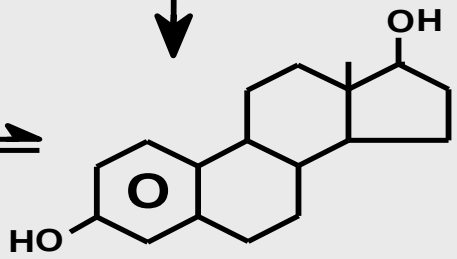
Tetosterone

Aromatase

Aromatase

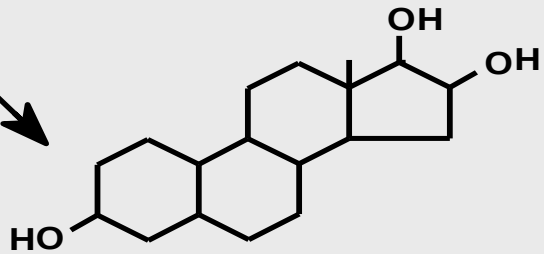


Esrone (E1)



Estradiol (E2)

Hydroxylation



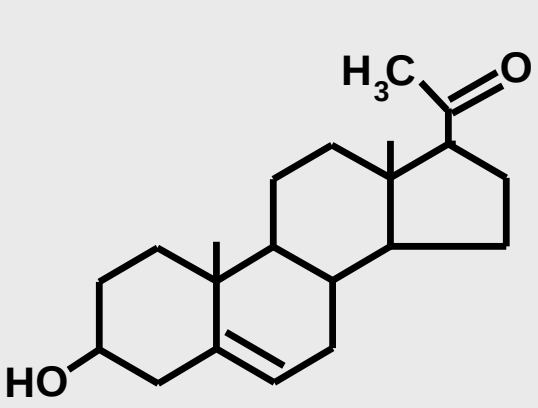
Estriol (E3)

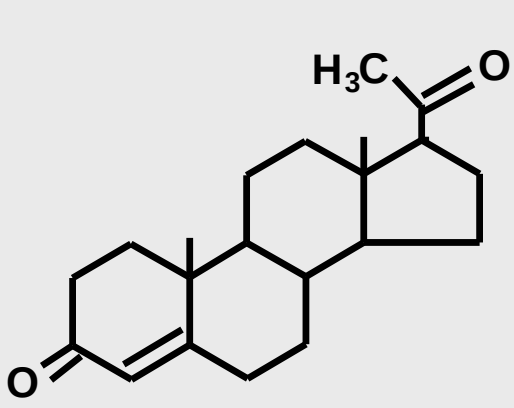
Urine of pregnency womem

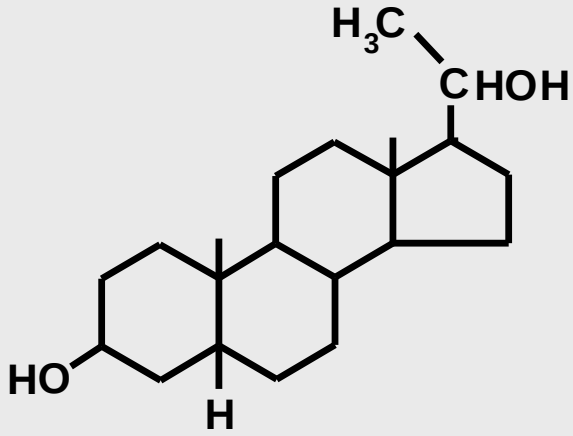
 # -Functions:- *- Follicular hormones prepare the uterine mucoses for latter action of progestational hormones. *- These actions include proliferation of the endometrium depening of glands, increased vascularity, etc. *- All these changes begin after cessation of menstral bleeding. *- They maintain female secondary sex characters acting against (antagonistic) testosterone.

(ii)- Progestrone hormone:- *- It is the hormone of **corpus leuteum**.

*- It is also formed by adrenal cortex and placenta.







Pregnendone → *Progestrone* → *pregnandiol*

 # -Functions:- ***-** This hormones appears after ovulation and causes extensive development of endometrium, thus preparing the uterus for reception of embryo, and for its nutrition. ***-** Progestrone also stimulates growth of the mamary glands. ***-** When pregnency occure, corpus leuteum is maintained, and **menstruation** and **ovulation** are suspended. ***-** the concentration of progesterone decreases near term. ***-** Progesterone has anti estrogenic effect on myometrium.

--It decreases excitability & sensitivity of uterus to oxytocin throughout pregnency.