



The Endocrine System



PHYSIOLOGY

☒ Sheet

☐ Slide

☐ Handout

Number: 5

Subject: Thyroid gland.

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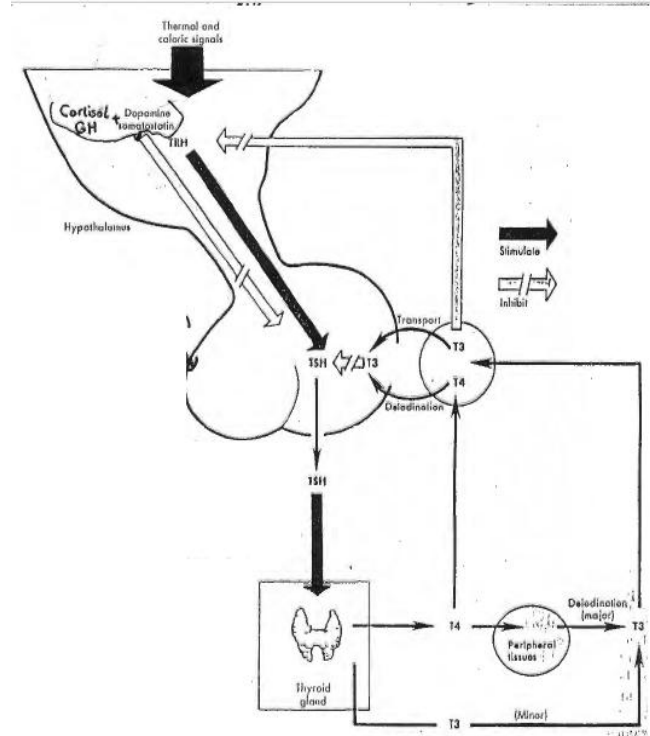
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physiology of Thyroid gland

- **Thyroid gland** is stimulated by **TSH** (thyroid-stimulating Hormone from the anterior pituitary gland) . TSH is stimulated by **TRH** (Tri-peptide hormone, a hypothalamic hormone) .
- **TRH** stimulate the synthesis, secretion and the bioactivity of the TSH .
- **TSH** stimulates the growth of the cell of thyroid gland as well as stimulates the synthesis and secretion of the thyroid hormones.
- **TSH is inhibited** by the Dopamine , Somatostatin inhibit , cortisol and growth hormone.
- Remember : **TRH stimulate TSH and prolactin**.



- TSH is glycoprotein and composed of two subunits (α , β).
 - 1) Alpha (α) is nonspecific, also found in other hormones; LH, FSH and CGH.
 - 2) Beta (β) is the specific, the active subunit; beta doesn't function unless it is bound with alpha.
- Thyroid gland simply produces **two active hormones T4 and T3**.
- T4 and T3 exhibit vital **mechanism on the pituitary level, thyroid level as well as hypothalamic level**.
- **Remember** that Hypothalamic hormones when they are released in the median eminence they remain in the nerve endings until they are stimulated .

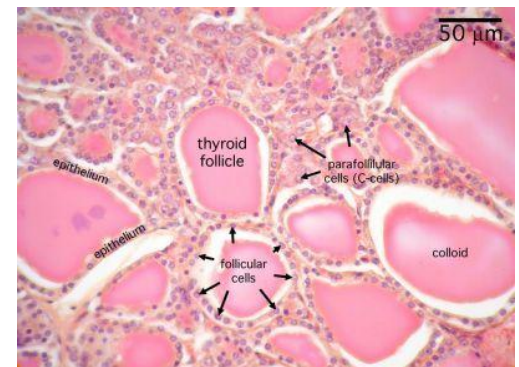
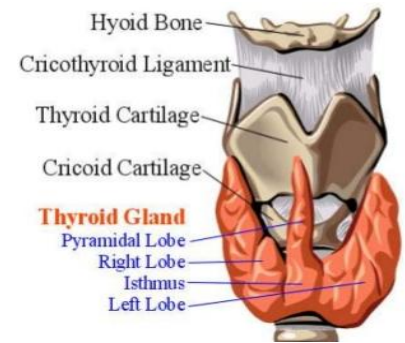
❖ TSH mechanism of action :

we said TSH is **glycoprotein** hormone and as we know protein hormones **either produce cAMP or activate phospholipase C and produce DAG and IP3 (2nd messengers)**.

- Most probably , TSH produces **cAMP** as a second messenger for the **synthesis and secretion of the hormone**.
- Activation of the **phospholipase C** to produce the two second messengers: DAG and IP3. – for the **metabolism of the thyroid cells**.

❖ Thyroid Gland anatomy ,histology and embryology :

- Thyroid gland is composed of two lobes (right and left) joined together by isthmus .
- The weight of thyroid gland is about 30 g.
- At 12 week of gestation , the thyroid gland and pituitary gland begin to function . the fetal thyroid hormones are important for normal development of the nervous system and skeleton.
- The production of the thyroid hormones is under the effect of the fetal anterior pituitary and the fetal hypothalamic hormones because the maternal hypothalamic hormones as well as the pituitary hormones as well as thyroid hormones cannot pass from the maternal blood to the fetus.>>> very very important .
- If we take a section from thyroid gland , we find that it's composed of follicles lined by cubical cells (epithelial cells) , in between there are parafoollicular cells (these cells produce unrelated hormone >>> calcitonin which decrease the calcium plasma level).
- The follicles are full of colloid (water, proteins ,hormones ,enzymes ,, etc).



✚ Thyroid gland is a unique gland in two things :

1. The only gland in the body that incorporates **inorganic substance (iodine) with organic substance (the amino acid tyrosine)** during the synthesis of the hormones .
2. The only gland that can synthesize hormones and store them **sufficiently for more that 1 month . some studies say that the storage of hormones belong for 3 months.**
 - ✓ If we isolate thyroid gland by cutting the blood supply , the patient won't need thyroid hormones supplement for 2-3 months.

❖ Thyroid hormones:

- There are three types of thyroid hormones : **T3, T4 , rT3.**
- Any of the thyroid hormones is composed of **tyrosine** .
- Now let's see the formation of these hormones and the characteristics of each on in more details .

- When tyrosine binds 1 iodine this produces **mono-iodotyrosine**. When tyrosine binds 2 iodine this produces **di-iodotyrosine**. This is called **iodination**.
- **Iodination** (aka organification) : addition of iodine to the tyrosine .
- -When **mono-iodotyrosine** binds with **di-iodotyrosine** produces hormone called **T3 or tri-iodothyronine**. This is called **coupling** .
- -When **di-iodotyrosine** binds another **di-iodotyrosine** produces thyroid hormone called **thyroxine or T4 or tetra-iodotyrosine**. This is called **coupling** .
- **coupling** : binding of **mono-iodotyrosine** with **di-iodotyrosine** or binding of **di-iodotyrosine** binds with **di-iodotyrosine**.

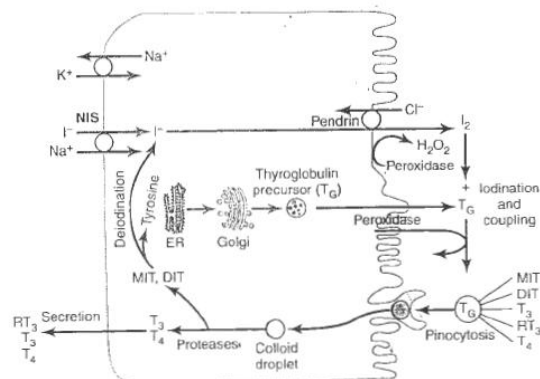
✓ The formation of thyroid hormones involve Iodination and Coupling.

- Sometimes, during the **metabolism of the T4** an inactive form is produced and it's called reverse T3 (rT3) . Reverse T3 is similar to T3 but the difference is in the **location of iodine on the tyrosine**.
- Thyroid gland produce 3 hormones **mainly T4 , little T3 and very little rT3**.
- **T4** is a **pro hormone** produces the other hormones , its **activity is very little and sometimes it's inactive** .the **most active is T3** and totally **inactive is rT3**.

❖ Synthesis and the secretion of the thyroid hormones:

- Synthesis needs iodine, iodine is taken from the **plasma or from inside the cells**, then iodine is taken inside the follicular cells through iodide pump or Na^+/I^- co transport (active transport) . in the follicular cell membrane there are peroxidases that oxidase the I^- into I_2 .
- the follicular cells inside the thyroid gland produce a protein **called thyroglobulin** , which is composed of **amino acids Tyrosine ranged in 100- 120** (the number is varied between individuals).
- the iodination and coupling **don't occur on free tyrosine** , but occur on the tyrosine in the structure of thyroglobulin .
- in the thyroglobulin not the 100 tyrosine bind to iodine just 70 bind to iodine .
4-8% of the 70 tyrosine produce thyroid hormones.
- Iodination and coupling occur to the tyrosine in the Tg .
- Tg carry **T4, T3, rT3, DIT and MIT**.

Then by **pinocytosis** enter into the cells . inside the cells under the effect of enzymes (proteases) these hormones become free . **then the hormones (T4, T3, rT3) are released into the blood to perform their function.**



❖ The metabolism of Thyroxin T4: -

- ✓ thyroid gland produces mainly T4 (pro-hormone).
- ✓ T4 either produces inactive substances rT3 or Tetrac (tetraiodoacetic acid). or produce active substance T3 or produce (DIT) di-iodothyronin.

❖ Thyroid hormone turnover :

- From the table , we can notice that all the T4 is produced from the thyroid gland , a little of T3 from and a very little of rT3.
- We can notice also, most of T3 and rT3 are produced from T4 .
- The doctor mentioned the plasma concentration (total , free) and the half life also.

■ Table 53-1 Thyroid hormone turnover

	T_4	T_3	rT_3
Daily production (μg)	90	35	35 ✓
From thyroid (%)	100	25	5 ✓
From T_4 (%)	—	75	95 ✓
Extracellular pool (μg)	850	40	40
Plasma concentration			
Total ($\mu\text{g/dl}$)	8.0	0.12	0.04 ✓
Free (ng/dl)	2.0	0.28	0.20 ✓
Half-life (days)	7	1	0.8 ✓
Metabolic clearance (L/day)	1	26	77
Fractional turnover per day (%)	10	75	90

Sorry for any mistake ^^.
Ayat M Zghoul.

Now a test with regard to the first 4 lectures !!!

- 1) One of the following is correct regarding classis hormones:**
 - a) They are secreted from endocrine glands into a duct.
 - b) They are usually secreted in the blood to affect nearby cells.
 - c) Acetylcholine is a good example.
 - d) Most are polypeptide hormones.
 - e) They can affect muscles to cause their contraction

- 2) Hormone X binds to an intracellular receptor of a target cell to induce lipolysis and reduce glucose uptake. One of the following doesn't correctly describe X.**
 - a) X is likely to activate a G protein coupled receptor
 - b) X, most probably, induces transcription of specific regions of DNA.
 - c) X has pleotropic effects.
 - d) X, most probably, affects many types of cells.
 - e) X must be bound to proteins in the plasma.

- 3) Binding of the hormone Y induces a cellular process 3-fold its induction of the same process after prolonged exposure of the cell to hormone Z. One of the following correctly describes Y.**
 - a) Y has desensitizing effects of the cell to Z.
 - b) Binding of Y causes homologous desensitization of the cell.
 - c) Z antagonizes the effects of Y.
 - d) Z decreases the number of receptors of Y on the cell.
 - e) Both c+d are correct.

- 4) One of the following hormones doesn't bind to a membrane receptor.**
 - a) Thyroxine.
 - b) Norepinephrine
 - c) Epinephrine
 - d) Thyroid stimulating hormone
 - e) Glucagon

- 5) Secretion of a hormone further increased its secretion in the blood. One of the following correctly describes the hormone:**
- a) The stimulus-response is Hormone-Hormone.
 - b) It's possible that the affinity of the receptor of the hormone is decreased.
 - c) It's possible that the hormone exhibits positive feedback mechanism.
 - d) Both a+b are correct.
 - e) All a+b+c are correct.
- 6) Hormone A inhibits the release of the hormone that affected the gland which secreted it:**
- a) This is an example of the positive feedback mechanism.
 - b) This is an example of short loop feedback.
 - c) It's possible that Hormone A is oxytocin.
 - d) The gland that secreted the hormone A possesses the receptor of the hormone A.
 - e) More than one is correct.
- 7) Knowing that ACTH is necessary for the secretion of aldosterone. One of the following is true:**
- a) The interaction is called synergism.
 - b) To secrete more amounts of aldosterone, more ACTH is required.
 - c) ACTH is sufficient to cause aldosterone secretion.
 - d) All are correct.
 - e) Nothing is correct
- 8) One of the following is not a characteristics of peptide hormones:**
- a) They usually increase intracellular second messengers' concentrations such as cAMP, Ca^{2+} , PI3, DAG.
 - b) Their action is always fast and prolonged.
 - c) They can't cross cell membranes.
 - d) Some are glycoproteins.
 - e) They play a very important role in the growth process.

9) One of the following is true about the pituitary gland and its hormones:

- a) The posterior pituitary synthesizes 2 hormones, oxytocin and ADH.
- b) Some neurons in the hypothalamus secrete neurohormones directly into the blood.
- c) ADH is secreted in response to decreased extracellular fluid osmolarity.
- d) Increased Na^+ reabsorption caused by ADH increases blood pressure.
- e) More than one is correct.

10) One of the following is correct regarding the anterior pituitary and the hypothalamus:

- a) Growth hormone and prolactin are both secreted from somatotropes
- b) The only cell type of the anterior pituitary that secretes two major hormones is gonadotropes.
- c) The only hypothalamic hormone which has an inhibitory effect is FSH.
- d) Hormones from the hypothalamus reach it by either long or short portal vessels, depending on the rapidity needed for the effects.
- e) All are correct

11) One of the following is not correct regarding parturition and uterine contractions:

- a) Estrogens and not oxytocin are responsible for the initiation of parturition.
- b) Estrogens stimulate oxytocin secretion.
- c) Cervical stretching stimulates oxytocin secretion
- d) Prostaglandins stimulate uterine contractions.
- e) All are correct.

12) One of the following chemicals doesn't play a role in the growth process:

- a) Insulin
- b) Somatomedin C
- c) Aldosterone
- d) Thyroxine
- e) Cortisol

13) One of the following is not correct about growth hormone:

- a) Spares proteins.
- b) Increases lipolysis.
- c) Excess may cause ketosis and acidosis.
- d) Inhibits release of insulin from the pancreas.
- e) All are correct.

14) One of the following statements is not true regarding growth hormone:

- a) Has a synergistic effect with insulin.
- b) Its secretion is increased after a carbohydrate-rich meal.
- c) Its secretion is inhibited in diabetic patients.
- d) Somatomedins inhibit its secretion.
- e) Its secretion is increased in fasting individuals and after a strenuous exercise.

15) One of the following statements is incorrect regarding ACTH:

- a) It has an important role in stimulation of the secretion of adrenal androgens, especially after puberty.
- b) α subunit is necessary for its activity.
- c) Its target zone is zona fasciculata.
- d) Its secretion is inhibited by cortisol
- e) All are correct.

16) Cortisol doesn't have an important contribution to the mineralocorticoid activity because:

- a) Cortisol can't bind to MR receptor.
- b) Cortisol concentration in the blood is lower than aldosterone.
- c) Kidney's epithelial cells convert cortisol to corticosterone.
- d) Cortisol can't enter the cell to bind the receptor.
- e) None of the above is correct.

17) A good indicator of 11 β -hydroxylase (converts 11-deoxycortisol to cortisol) deficiency is:

- a) Increased level of corticosterone.
- b) Increased level of aldosterone.
- c) Decreased level of androgens.
- d) Increased level of deoxycortisol.
- e) More than one is correct.

18) One of the following is correct about cortisol:

- a) Its effects in protein and fat metabolism aren't as important as its effects on carbohydrates metabolism.
- b) Only 6% of the plasma cortisol is free.
- c) Has a relatively long half-life.
- d) Its level reaches its peak at 12:00 PM.
- e) Important during fasting but not essential in fetal life.

19) One of the following is not an effect of cortisol:

- a) Potentiates the effects of glucagon and epinephrine.
- b) Increases hepatic protein mobilization.
- c) Conserves glycogen stores.
- d) Responds to many types of stresses.
- e) All are correct.

20) One of the following doesn't stimulate aldosterone secretion at all:

- a) Angiotensin 2 and 3.
- b) Decreased Na^+ delivered to the kidneys.
- c) Increased intracellular K^+ concentration.
- d) ACTH
- e) All are correct.

21) One of the following is not correct about adrenal androgens and estrogens:

- a) DHEA is a weak androgen.
- b) Estradiol is secreted from zona reticularis.
- c) They are the main responsible for female sexual characteristics
- d) A tumor in the adrenal cortex may cause their oversecretion.
- e) The most potent androgen is testosterone.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
D	A	D	A	E	B	E	B	B	C	B	C	D	B	A	C	D	C	B	C	C

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