University of Jordan - Faculty of Medicine
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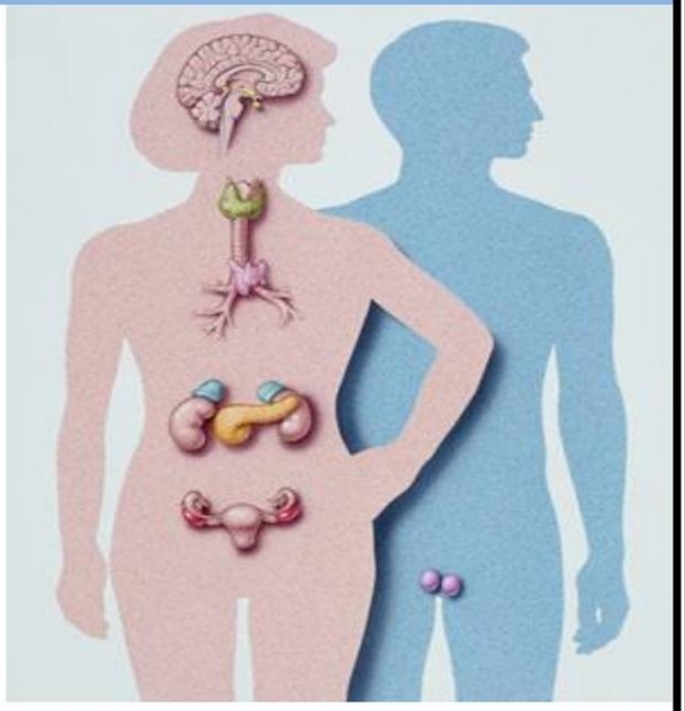
Medical Committee
The University of Jordan

Endocrine System



- ☐ Anatomy/Embryology/Histology
- ☐ Biochemistry
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- ☐ Pharmacology
- ☐ Pathology
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☐ Slide ■ Sheet ☐ Handout ☐ Other

Lecture #: **4**

Date:

Dr's Name: **Saleem**

Price:

Written by: **إيمان أحمد العموش**

Designed by: Zakaria W. Shkoukani

PHYSIOLOGY OF THYROID GLAND

-Thyroid gland is stimulated by TSH from the anterior pituitary gland. TSH is stimulated by TRH (Tri-peptide hormone), a hypothalamic hormone. TRH stimulates the secretion of TSH and also increases the bioactivity of the TSH.

-Dopamine and Somatostatin inhibit the TSH, also cortisol and growth hormone inhibits TSH but indirectly, most probably they stimulate the secretion of somatostatin.

-TSH stimulates the growth of the cell of thyroid gland as well as stimulates the synthesis and secretion of the thyroid hormones.

-TSH is a blood protein hormone composed of two subunits; Alfa and Beta:

1) Alfa is nonspecific, also found in other unregulated hormones; LH, FSH and CGH.

2) Beta is the specific, the active subunit; beta doesn't function unless it is bound with alpha.

-TSH stimulates the growth of the cell as well as the synthesis and the secretion of the thyroid hormones.

-Thyroid gland simply produces two hormones T4 and T3.

-T4 and T3 exhibit blood control on the pituitary level, thyroid level as well as hypothalamic level.

-You remember the negative feedback control; the relationship between the stimulus and the response.

-TSH produces cAMP as a second messenger for the synthesis and secretion of the hormones and also activates the phopsolipase C to produce the two second messengers: diaselglycerol and inositol tri phosphate.

-Most probably the production of these two second messengers for the metabolism of the thyroid cells.

-Thyroid gland is composed of 2 lobes (right and left), joined by a part called isthmus which lies in front of the trachea. The weight of the thyroid gland differs from person to person, but within average it weights between 25-30 gm and its rich in blood supply which means the thyroid gland is very important.

-By the 12^{th} week of gestation the fetal thyroid gland produces thyroid hormones. These hormones are essential 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 the placenta to the fetus. (This point is very important).

-You remember from histology that the thyroid gland is composed of follicles.

-In the follicle there is colloid (colloid fluids, proteins, hormones, enzymes etc).

-There follicles are encircled with the thyroid epithelial cells.

-These epithelial cells synthesize the hormones.

-Between the follicles there are cells, parafolicular cells, unrelated cells they produce unrelated hormones.

-These cells produce **calcitonin** which functions on the calcium level in the blood.

-Thyroid gland is unique in 2 aspects:

First: Thyroid gland produces hormones and these hormones are stored in the colloid, sufficient for the human being for at least one month.

Second: The only gland during the synthesis of the hormones incorporates inorganic substance (iodine) with organic substance (the amino acid tyrosine).

-When tyrosine binds 1 iodine this produces mono-iodotyrosine. This is called **iodination.**

-When tyrosine binds 2 iodine this produces di-iodotyrosine.

-Maximally the tyrosine carries 2 iodine.

-When di-iodotyrosin binds another di-iodotyrosine produces thyroid hormone called thyroxin or T4 or tetra-iodotyrosine.

-Maximally thyroid hormone carries 4 iodine.

-When mono-iodotyrosine binds with di-iodotyrosine produces hormone called T3 or tri-iodothyronine.

-Either in T4 or T3 there is coupling between the iodinated tyrosine.

-The thyroid gland produces the iodothyronin the hormone and iodotyrosine the iodinated amino acids.

-Mainly thyroid gland produces T4, this T4 after the production through the effect of enzymes produces either T3 or reverse T3 (rT3).

-Reverse T3 is similar to T3 but the difference is in the binding of iodine with the tyrosine.

-Thyroid gland produces mainly T4 (pro hormone) which produces -in need- T3 the most active hormone, but when there is no need, it produces reverse T3.

→T3 is the most active.

→Reverse T3is totally inactive.

→T4 either have little activity or no activity.

-Synthesis and the release of the thyroid hormones:

-Synthesis needs iodine, iodine is taken from the plasma or from inside the cells, then iodine is taken inside the epithelial cells, then bind there with depending carrier protein then enters into the colloid in the extent of chloride, this iodine is activated under the effect of peroxidase enzyme.

-Active iodine inside the colloid.

-Epithelial cells they produce a protein called thyroglobulin which contains about 70 tyrosine amino acids and they are the major substrates to combine with the iodine to form thyroid hormones.

-The thyroglobulin carrying 70 amino acids, there is difference between individual and another, there is no way we find the same structure of thyroglobulin from one person to person having the same number of amino acids ranging from 70 to 1 , 30 to 1 , 40 amino acids.

-In the structure 4 to 8% of the tyrosines they can bind iodine.

-you can understand the iodination and coupling don't occur on free tyrosine.

-iodine doesn't bind to tyrosine with free tyrosine in the colloid.

And also coupling doesn't occur on free tyrosine in the colloid.

-these two processes occur on tyrosine in the structure of thyroglobulin

-thyroglobulin carrying MIB, DIB, T4, T3 and rT3.

-In need these thyroglobulin are taken inside the cells under the effect of a process called pinocytosis.

-thyroglobulin carries all these lyses enzymes inside the cell which lyses the thyroglobulin to release reverse T3, rT3 and T4.

-normally just the hormones are released into the blood.

Abnormally we see thyroglobulins and myc and dyc .

Iodination and coupling don't occur unless thyroxin is bound or in the structure of thyroglobulin.

- The metabolism of Thyroxin T4:

-Thyroid gland produces mainly T4 (pro-hormone).

-T4 either produces T3(when needed),reverse T3(when there is no need), then these they produce (DIT) di-iodothyronin or totally t4 produces inactive substance, the same structure but T4 is inactivated and it's called Tetrac (tetraiodoacetic acid).

-Thyroid hormone turnover:

Table #1	T4	T3	rT3
Daily production	90%	35%	35%
→From thyroid	100%	25%	5%
→From T4	----------	75%	95%
Plasma concentration			
→Total	8.0	0.12	.04
→Free	2.0	.28	.20
Half life(day)	7	1	0.8

-Thyroid hormone binding protein:

-We need the thyroid hormones bound to proteins; because thyroid hormones are very dangerous in the body when they are free.

-99.5 % of T3 is bound to proteins.

-99.98% of T4 is bound to proteins.

-Three types of proteins are bound to thyroid hormones:

1. **TGB** (thyroid-binding globulin).
2. **Albumin**.
3. **TBPA** (thyroxin-binding prealbumin).

Table #2	Actual binding T4 %	Actual binding T3 %
TBG	75	75
Albumin	10	25
TBPA	15	0

-Check the percentage table #2 at the right.

-T3 doesn't bind to TBPA.

-Being bound with plasma proteins has two advantages:

1) Preventing the filtration of the hormones through the glomeruli.
2) Prolong the half life of the hormones.

-Thyroid hormone intracellular actions and whole body effects:

-You remember when we talked about the amino acid derivative hormones: Catecholamine and thyroid hormones. Catecholamine hormones cannot penetrate cell membrane.

-Thyroid hormones can penetrate the cell membrane→they bind the receptor inside the cell membrane or nuclear membrane → activating DNA →producing MRNA→producing physiological responses:

1. Increasing Na+, K+ ATPase. 2. Increasing respiratory enzymes.

3. Increasing other enzymes and proteins. 4. Protiens for growth and maturation.

→All these results require:

1. Increase of consumption of oxygen which requires: a) Increasing cardiac output. B) Increasing ventilation.

2. Taking substrates, then subsequently: a) Increasing food intake. B).increasing mobilization of carbohydrates, proteins and fat.

→The end result: 1) Increase CO2. 2) Increase thermogenesis.

This is simply the overall function of thyroid hormones.

-Factors Affecting thyroid hormone secretion:

Stimulatory Factors	Inhibitory Factors
TSH. Thyroid-stimulating immunoglobulins. Increased TBG levels (e.g., pregnancy).	Iodine deficiency. Deiodinase deficiency. Excessive Iodine intake (Wolff-Chaikoff effect). Perchlorate; thiocyanate (inhibit iodine pump). Propylthiouracil (inhibits peroxidase enzyme). Decreased TBG levels (e.g., Liver disease).

"If it is important enough to you, you will find a way. If it is not, you will find an excuse."

Written by: Eman Ahmad.