The Endocrine System

PHYSIOLOGY

☑ Sheet ☐ Slide ☐ Handout

Number:	6
Subject:	Thyroid gland-2
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Price:

Review:

●Thyroid gland is an endocrine gland located in the neck anterior to the trachea. It's composed histologically from many follicles that are filled with colloid material. This gland secretes thyroid metabolic hormones; T3 and T4, T3 is more active than T4.Thyroid gland, in general, controls our metabolic activity and heat production, as well as the development of the CNS and MSS.

●Thyroid gland is unique in 2 aspects:

1- Thyroid gland produces hormones and these hormones are stored in the colloid, sufficient for the human being for at least one month.
2- The only gland during the synthesis of the hormones incorporates inorganic substance (iodine) with organic substance (the amino acid tyrosine).

●The production of the thyroid hormones is under the effect of the fetal anterior pituitary and the fetal hypothalamic hormones, due to the fact that babies with congenital problems in thyroid or pituitary gland develop symptoms of hypothyroidism; growth delay and mental retardation.

This occurs because maternal hypothalamic hormones, pituitary hormones as well as thyroid hormones cannot pass the placenta to the fetus.

Thyroid hormone binding protein

●Due to the fact that thyroid hormones are lipid soluble, these hormones must be bound to proteins. Moreover, 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:

- TBG (thyroxin-binding globulin).
- Albumin.
- TBPA (thyroxin-binding prealbumin).

●Check the percentage table and notes below:

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

- T3 doesn't bind to TBPA.
- Being bound with plasma proteins has two advantages:
  1- Preventing the filtration of the hormones through the glomeruli and maintain thyroid hormone concentration in plasma.
  2- Prolong the half life of the hormones.

Thyroid hormone intracellular actions and whole body effects:

●due its lipophilicity, it affects all our cells.

●thyroid hormone intracellular action is a good example of lipid soluble hormones signaling pathways:

1- Thyroid hormones can penetrate the cell membrane
2- They bind the receptor inside the cell membrane or nuclear membrane
3- activating DNA.
4- producing mRNA.
5- producing physiological response.

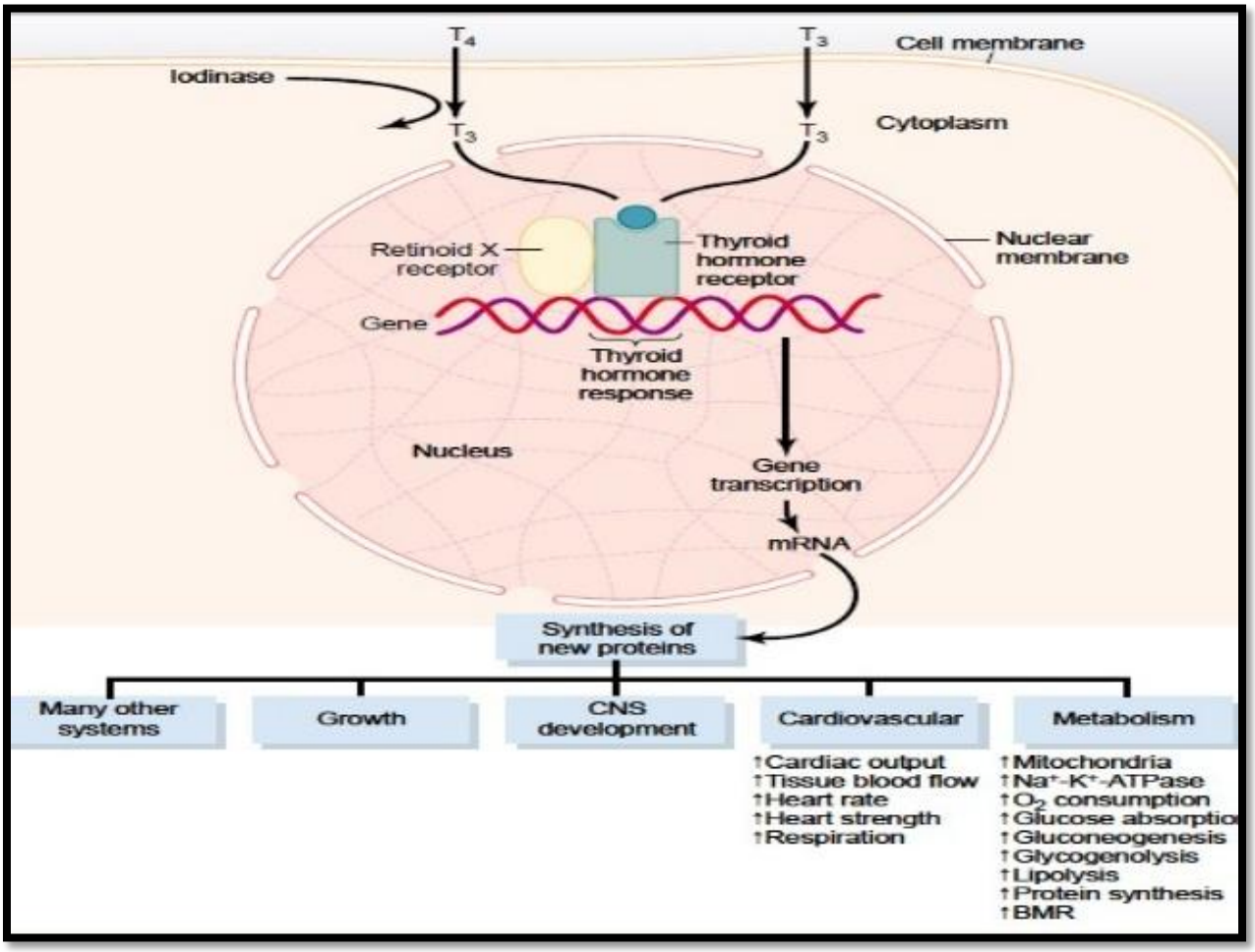
●Physiological responses are due to gene expression of many enzymes, thus activating all metabolic activities, major responses are:

- Enhance cellular metabolic activities by increasing Na+, K+ ATPase, Increasing respiratory enzymes as well as Increasing other enzymes and proteins for growth and maturation.

- This leads to Increase in consumption of oxygen by Increasing cardiac output as well as Increasing ventilation.
- Also, this requires taking substrates, then subsequently Increasing food intake and increasing mobilization of carbohydrates, proteins and fat.
- The end result isIncreasingCO2 production and increasing thermogenesis.

●Note: for more details refer to Guyton and Hall or check thyroidvideo.

●the figure below summarizes thyroid hormone functions and mechanism of action:



Factors Affecting thyroid hormone secretion

●We said that TSH and TRH regulate thyroid gland activity, however, there are some exogenous factors that affects thyroid gland activity, summarized in this table:

Stimulatory Factors	Inhibitory Factors
●TSH ●Thyroid-stimulating immunoglobulins (as seen in Graves' disease. ●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).

●Notes :

- Thyroid hormone along with other hormones (Insulin-like growth factor-I "IGF-I", insulin, cortisol, androgens and estrogens) contribute to the growth process in humans. But GH and IGF-I have been implicated as the major determinants of growth in normal post uterine life (after birth).
- Thyroid Hormones are essential in normal amounts for growth, excess doesn't produce overgrowth as with GH, but causes increase catabolism of proteins and other nutrients. But if these thyroid hormones are deficient, many processes in the body will be disturbed. ***"no growth without energy***".
- Normal concentrations of thyroid hormones are very low and the total T4 in adults is approximately (8mcg/dl),while free T4(not bound to protein)is only .03% which is (2ng/dl).Total T3 is (0.12 mcg /dl) and free T3 is .3% that is (0.28 ng/dl).
- Thyroxine (T4) at normal concentration has permissive effect on the action of GH on protein synthesis. So, in its absence, amino acids uptake and protein synthesis are not much stimulated.

Clinical applications

1-Pituitary dwarfism vs. cretinism

●Reduced thyroid activity in childhood produces dwarfs who are mentally retarded, whereas reduced GH in childhood produces dwarfs (short stature) with normal intelligence.

- ***Cretinism*** (aka thyroid dwarfism, to differentiate between it and the dwarfism caused by growth hormone deficiency) is a condition arising from the deficiency of thyroid hormone. The fetus fails in developing skeletal, mental and sexual abilities.
- ***Pituitary dwarfism*** is caused by inadequate amounts of growth hormone .Growth hormone deficiency results in abnormally slow growth and short stature with normal proportions.

2- Hypothyroidism

●**Hypothyroidism** means under activity of thyroid, The most common causes are:iodine deficiency, surgical removal of your thyroid, autoimmune diseases, and radiation treatment.

●The main symptoms are :

- **Cretinism**: Associated with hyposecretion of thyroid hormone during childhood, It is characterized by: dwarfism; failure of skeletal, sexual and mental growth and development.

- **Myxoedema**: During adulthood, It's characterized by slowing down of all bodily processes; this is because of thyroid hormone deficiency. Here, The body processes that are slowed down (ex: *Tissue oxidation, Gut movements, Basal Metabolic Rate (BMR), Heart and Respiratory Rates, Body temperature falls, Thought processes, Blood Cholesterol increases, Slow husky voice, Appetite is reduced, Hair-Brittle, dry*)

3-Hyperthyrodisim

●Causes: increased production of thyroid stimulating immunoglobulins(TSI) (Graves' disease), secondary to excess hypothalamic and pituitary secretion, hypersecreting thyroid tumor (Adenoma).

●The main symptoms are:

- **Exophthalmos**: The protrusion of the eye balls. Most but not all patients with hyperthyroidism develop some degree of protruding of eye balls, It usually occurs due to increased production of antibody called Thyroid Stimulating Immunoglobulin (TSI) which acts against a protein of the extraocular muscles and the connective tissue behind the eye which causes these tissues to swell, It is not due to an excess of the thyroid hormones.

- **Goiter:**The enlargement of the thyroid gland. It does occur in both hypothyroidism and hyperthyroidism because of the continuous stimulation of thyroid cells. Sometimes, goiter occurs along with exophthalmos , but not necessarily in all cases. It may occur alone.

●**Note#1:** Having a goiter doesn't necessarily mean that your thyroid gland isn't working normally. Even when it's enlarged, your thyroid may produce normal amounts of hormones. It might also, however, produce too much or too little thyroxine and T3.

●**Note#2:** Exophthalmos occurs only in case of Hyperthyroidism.

●**Note#3 :**there are two types of goiter:

- **Simple benign (nontoxic)**: in which T3 and T4 levels are low, A non-cancerous enlargement of the thyroid gland is called a simple goiter and can form as a diffuse or as a nodular goiter.
- **Malignant (toxic)**: in which T3 and T4 levels are high. Toxic goiters are an enlargement of the thyroid gland resulting from an overproduction of the thyroid hormone, a condition called hyperthyroidism.

●**Graves' disease**, Also known as toxic diffuse goiter. It frequently results in hyperthyroidism and an enlarged thyroid.

●**Note**: this table summarizes the major types of thyroid dysfunction, you have to be familiar with it.

Thyroid dysfunction	Causes	Plasma concentration of relevant hormones	Goiter present?
Hypothyrodism	-Primary failure of thyroid gland	-↓T3&T4,↑TSH	**Yes**
	-Secondary to hypothalamic or anterior pituitary failure	-↓T3&T4,↓TRH and/or ↓TSH	No
	-Lack of dietary iodine	-↓T3&T4,↑TSH.	**Yes**
Hyperthyrodism	-Abnormal presence of thyroid stimulating immunoglobulin TSI (Grave's disease)	-↑T3&T4,↓TSH.	**Yes**
	-secondary to excess hypothalamic or anterior pituitary secretion	-↑T3&T4, ↑TRH and/or ↑TSH	**Yes**
	-Hypersecreting thyroid tumor	-↑T3&T4,↓TSH.	No

●important notes regarding this table (not mentioned by the doctor):

- Any deficiency in T3 and T4 caused by problems in thyroid gland itself will elevate TSH concentration.
- Any problem in TSH and TRH will decrease T3 and T4 concentration.
- Overactivation of thyroid gland with primary deficiency in T3 and T4 will cause goiter.
- Autoactivation of thyroid gland will elevate T3 and T4, but TSH levels will decrease.
- All hyperthyroidisms are associated with enlargement of the gland (tumor or goiter).

4-Hyposecretion of Pituitary gland

A) **Panhypopituitarism** (deficiency of all pituitary hormones as if you removed the whole gland) results in:

- diabetes insipidus because of ADH deficiency (water isn't reabsorbed back to the blood , excretion a lot of urine). It's similar to diabetes mellitus but the urine in diabetes insipidus is pale but in diabetes mellitus the urine is dark.

- Absence of gonadotropins (FSH/ LH):

  - **In males**: no testosterone, decreased libido (sexual desire) , NO sperms, loss of body hair.
  - **In females**: no progesterone and estrogen ,decreased libido and amenorrhea (NO menstrual cycles).

- TSH deficiency causes atrophy of thyroid gland.

- ACTH deficiency causes atrophy of adrenal cortex.

- MSH (melanocyte-stimulating hormone) deficiency →pallor color.

- GH (somatotropin) deficiency causes dwarfism (it affects sexual ability and fertility), the mental ability isn't affected significantly.

B)Severe anterior pituitary deficiency:

It's similar to Panhypopituitarism except those of the post. Pituitary hormones are normal. So sexuality, thyroid, adrenal cortex, color and also tall (dwarfs) will be affected.

C)Moderate anterior pituitary deficiency:

Gonadotropins & TSH are deficient; ACTH & MSH are partially deficient, GH is normal.

D)Mild anterior pituitary deficiency:

Only Gonadotropins are deficient ,the others are normal.

NOTE: we can notice that in ALL conditions "A→D" Gonadotropins are deficient, So gonadotropins are affected in both moderate and mild anterior pituitary deficiencies.

●Best wishes.

●The end