

Lecture Notes

UJ | SCHOOL OF MED

PHYSIOLOGY

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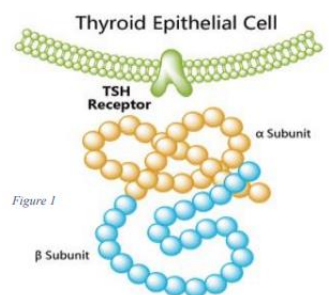
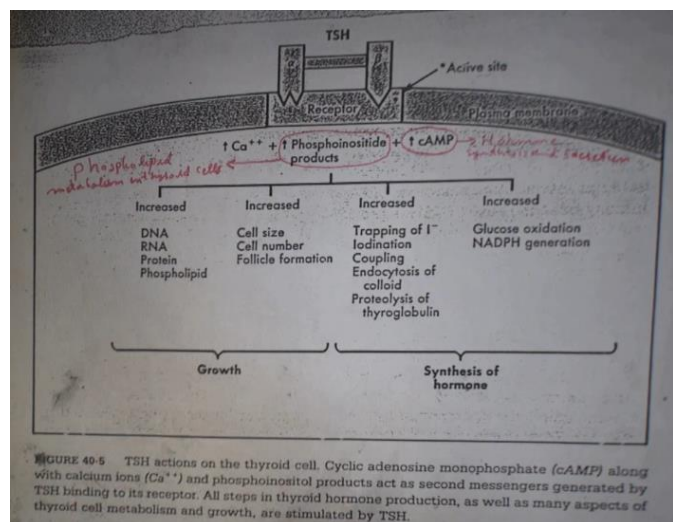
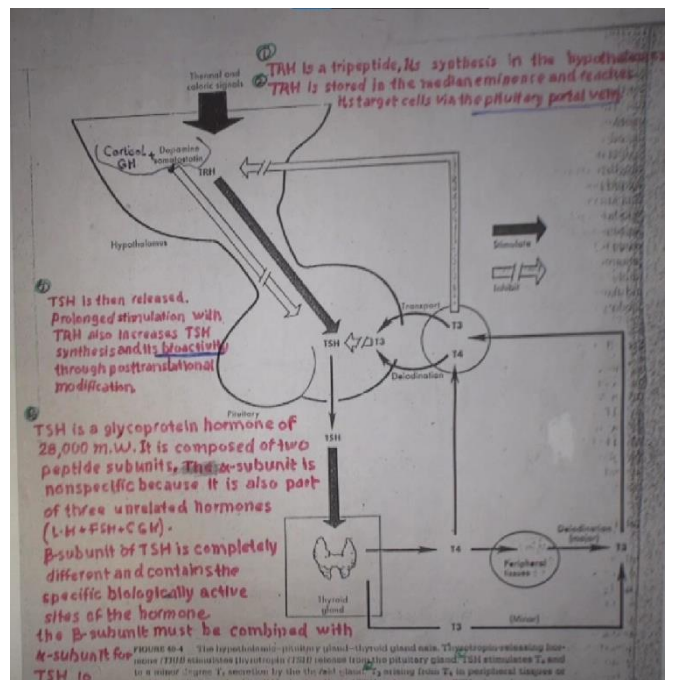


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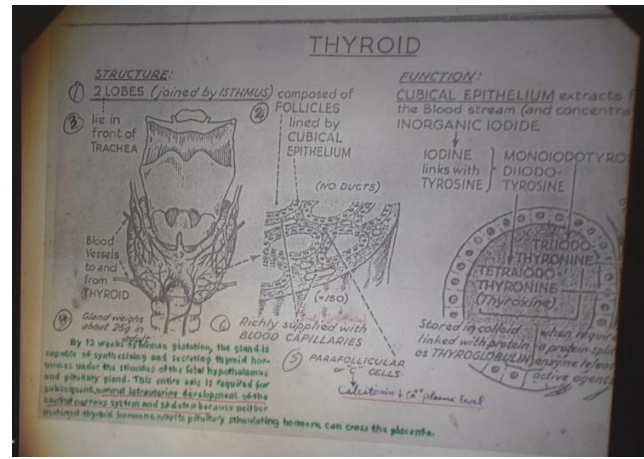
Physiology Lecture 7

- You should know by now that the thyroid gland is stimulated by **TSH** (glycoprotein) which is secreted by the **anterior pituitary gland**.
- TSH itself is stimulated by **TRH** (tripeptide) which is synthesized in the **hypothalamus**.
 - Firstly TRH is released into the median eminence (part of the hypothalamus from which regulatory hormones are released)
 - Then it affects the pituitary gland (through the pituitary portal vein) to secrete TSH.
- TSH hormone stimulates the growth of the thyroid gland as well as the production of its hormones (**synthesis and secretion**).
- NOTE : I actually recommend you read what's written inside this figure .
- TSH is inhibited by hormones like :
 - Dopamine.
 - Somatostatin.
 - Cortisol.
 - Growth Hormone.
- Thyroid Gland produces hormones like T3 , T4 (we'll explain these later on) .
- TSH is composed of 2 subunits:
 - an α (nonspecific or nonfunctional) subunit .
 - a β (specific or functional) subunit , it's the active site , BUT , it won't function unless it's bound to α .
- from the previous figure , you can conclude that when TSH binds to its receptor in the membrane of thyroid cells it causes the production of :
 - cAMP
 - 2 second messengers in the cytosol (IP3, DAG).
- cAMP is most probably used for the **synthesis and releasing of thyroid hormones**, while the other two messengers are for the **metabolism of the gland**.

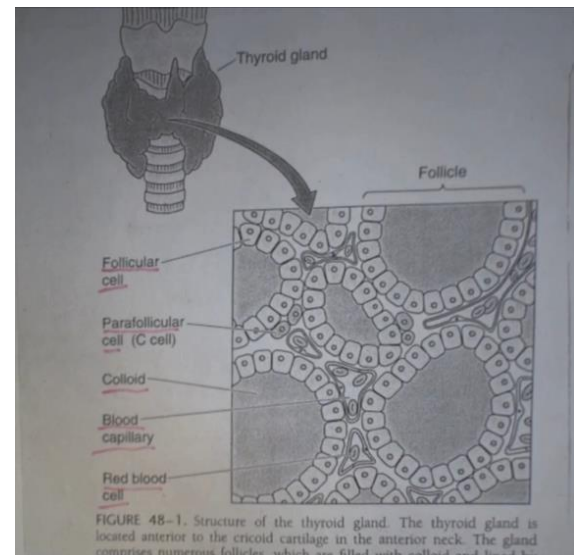


Thyroid Gland

- Thyroid gland lies in front of the trachea & weighs about 25 g in adults .
- Composed of right and left lobes joined by a part called isthmus .
- It has a rich blood supply (EXTRA : this indicates the importance of the gland) .
- Thyroid hormone is essential for life , starting with fetal life . therefore the production of fetal thyroid hormones begins very early .

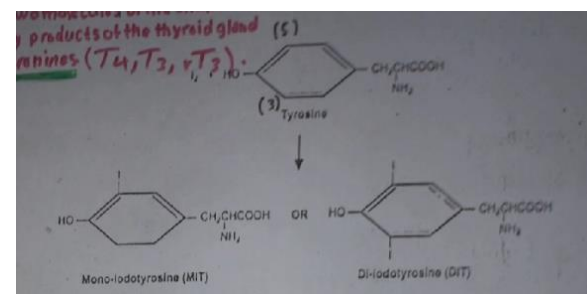


- by 12 weeks of gestation , the gland of the fetus is capable of synthesizing and secreting thyroid hormones under the stimulus of the fetal hypothalamus & pituitary gland .
- this entire axis is required for subsequent normal intrauterine development of the CNS & skeleton because neither the maternal thyroid hormones nor it's pituitary stimulating hormone can cross the placenta even though they're small. (EXTRA : so any deficiency in the thyroid hormones during this period will lead to developmental problems in these two systems) .
- In histological sections taken from the thyroid gland , we find that the section is composed of follicles, which are filled with fluids (fluids full of proteins, enzymes, electrolytes, ...etc.).
- These follicles are encircled by epithelial cells (or thyroid cells or follicular cells), these cells synthesize the hormones and store them in the follicles.
- In between epithelial cells, there are parafollicular cells (or C cells) that produce an unrelated hormone known as calcitonin. It has a function related to the calcium .



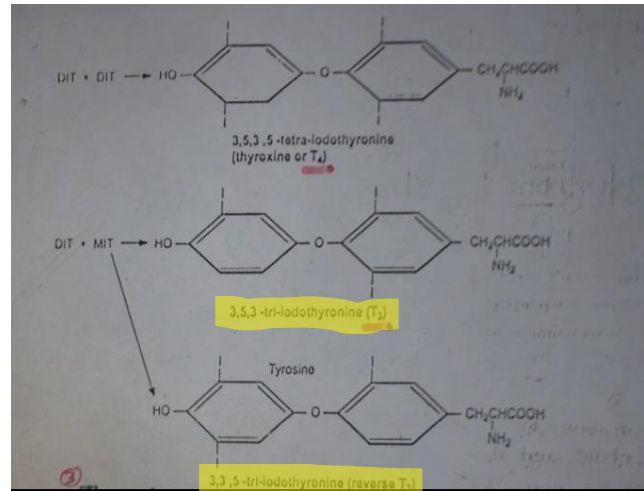
Thyroid Hormones

- They are composed of 2 Tyrosine residues, Tyr can bind iodine.
- Thyroid gland is unique , it's the only gland with 2 characteristics :



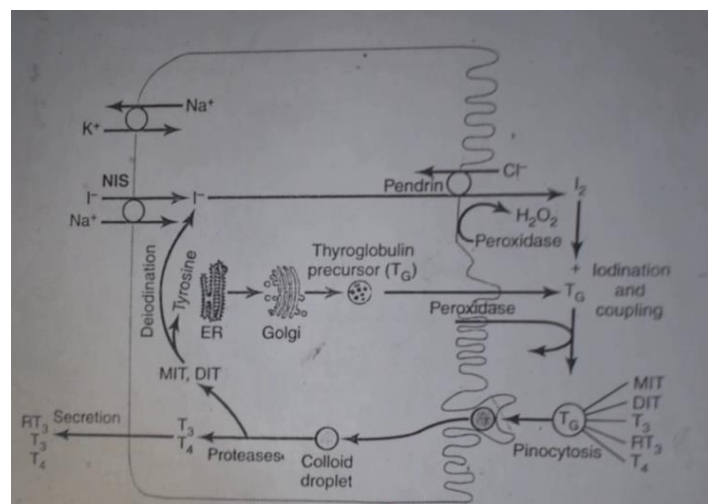
- It's hormones are unique in that they incorporate an inorganic element (iodine) into an organic structure made up of 2 molecules of the amino acid tyrosine (it is the only gland in the body that binds an inorganic substance with an organic substance) .
- The secretory products of the thyroid gland are known as iodothyronines (T₄ , T₃ , rT₃) . it's the only gland in the body to store hormones sufficient for the human body for about 2-3 months .

- When Tyr binds one iodine it produces what's called **Monoiodotyrosine (MIT)**, but when it binds two iodines it is called **Diiodotyrosine (DIT)**.
- Binding of Tyr with Iodine is called **Iodination** or **organification**.
- So you can understand from this figure that tyrosine maximally binds 2 iodines only.
- Remember, **thyroid hormones are neither proteins nor steroids, they're amino acid derivatives**.
- When **two DIT** bind with each other, they produce a hormone called **tetraiodothyronine** (or **Thyroxine** or **T4**). This is called **coupling**.
- When **one MIT** binds with **DIT**, they produce another hormone called **triiodothyronine** (or **T3**).
- There is a third hormone, which differs in the location of iodine on the bonds of Tyr, it is called **reversed T3 (RT3)**.
- Btw, T3 and T4 indicate the **number of Iodines**.
- So to sum up :



T4	T3	RT3
<ol style="list-style-type: none"> 1. The main one 2. has low activity (sometimes becomes inactive under the effect of some enzymes) 3. it is a prohormone (produces the other hormones T3 and RT3, and other products). 	<ol style="list-style-type: none"> 1. the most active one. (provides virtually all thyroid hormones activity) . 2. produced mostly in peripheral tissues from the prohormone T4. 3. secreted in less quantities than T4 . 	<ol style="list-style-type: none"> 1. totally inactive hormone.

- So, **iodination** is an **organic mutation** (binding of iodine to tyrosine), while **coupling** is binding of **two iodinated Tyr**. These two reactions (iodination and coupling) **don't occur on free Tyr in the colloid**.
- Iodine comes from the **plasma** or from the **cells themselves**. There are carriers for iodine and sodium; whenever the sodium enters, **iodine enters the cells along with the sodium**, then into the **colloid by another carrier (pendrin)**, which is **oxidized by peroxidase** to function and be used normally.
- Iodination & Coupling occur in the colloid, on the inner surface of epithelial cells, But, they don't occur on free tyr in the colloid.



(Iodination and coupling occur on Tyr in the structure of Thyroglobulin, but not all Tyr in the protein can bind iodine, about 4-8 of them only can bind)

- Epithelial cells of thyroid gland produce a protein called **Thyroglobulin**, which is composed of about 70 Tyr amino acids (ranging between 70-100 residues).

- *Thyroglobulin protein carries MIT, DIT, T3, T4, and RT3. When in need it is taken inside the cells by pinocytosis, then inside the cell it's lysed to release the hormones that are going to pass into the blood.*
- *EXTRA : Thyroid hormones (T3, T4) exert a negative feedback mechanism on the pituitary gland as well as on the hypothalamus.*
- *EXTRA : The storage of thyroid hormones (2-3 months) is different from the storage of iodine (6 months).*

Done By :

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