Thyroid Gland

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2nd STAGE

Physiology#II

Thyroid Gland

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- ***Overview***
- Thyroid gland is composed of two lobes connected by a narrow band of thyroid tissue (**isthmus**).The lobes are lateral to the upper portion of the trachea, inferior to the larynx.
- Thyroid gland is one of the largest endocrine gland with a weight of 20 gm.
- It is highly vascularized and appears more red than the surrounding tissues.
- It contains numerous small **sphere follicles.**.The center of each thyroid follicle is filled with proteins called **thyroglobulin**, which is synthesized and secreted by the cells of the thyroid follicles.
- Large amount of thyroid hormones are stored in the follicles as part of the thyroglobulin.
- Between the follicles there is a network of loose connective tissue which contains capillaries.
- There are scattered **parafollicles** among the follicles these parafollicles secrete **calcitonin.**
- **Calcitonin** regulates calcium level in the body fluid .It Reduce Ca^{2+} level in the body fluid when Ca^{2+}level become elevated.

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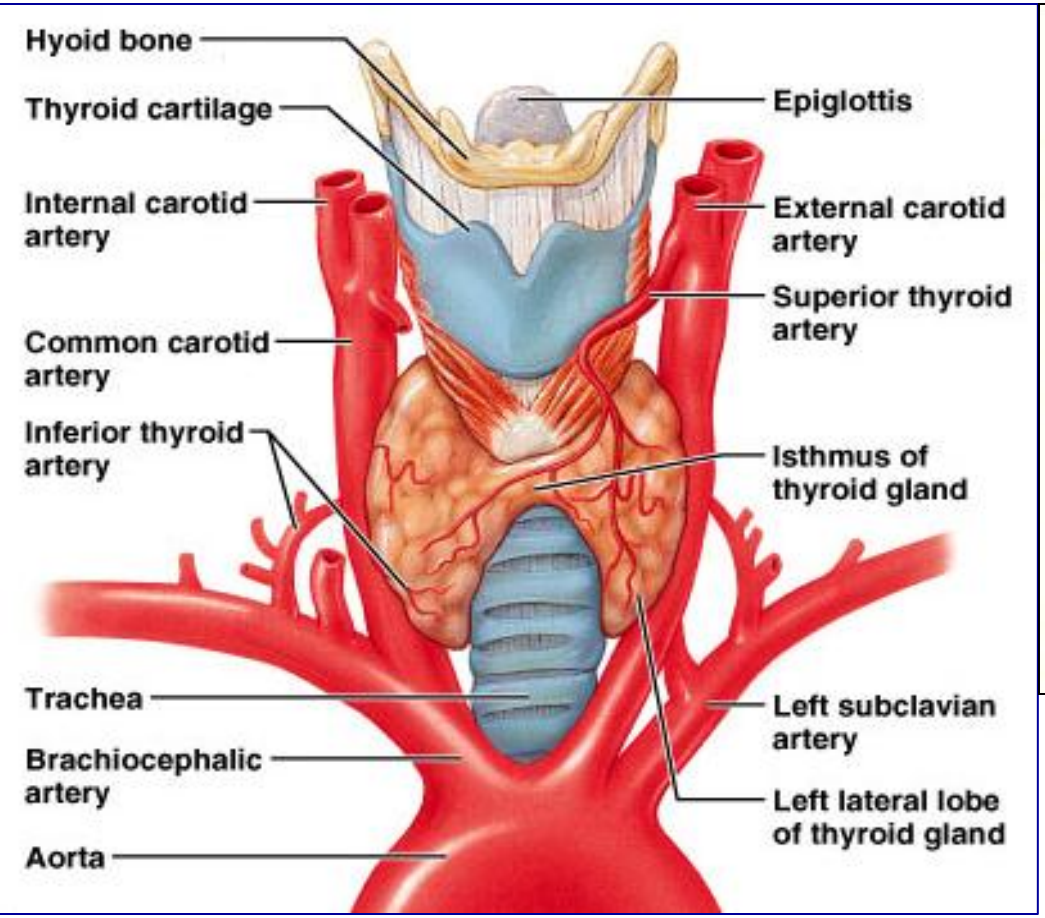

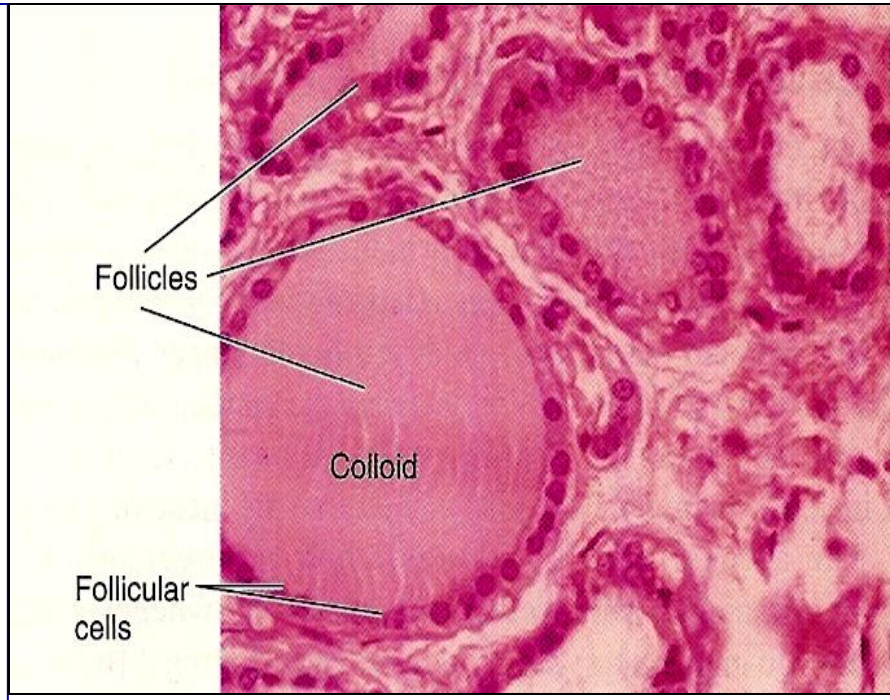

- **Thyroid Hormones**
- The major secretory products of the thyroid gland are:
- **Triiodothyronine (T3),** which constitutes 3-10% of the thyroid hormones.
- **Tetraiodothyronine or thyroxin (T4)** constitutes 90-97% of the thyroid hormones.
- **T3**and**T4** are of a clinical importance, secreted from the thyroid follicles.
- **Calcitonin**: is other hormone secreted by the **parafollicular cells** of thyroid gland.

Synthesis of T3, T4

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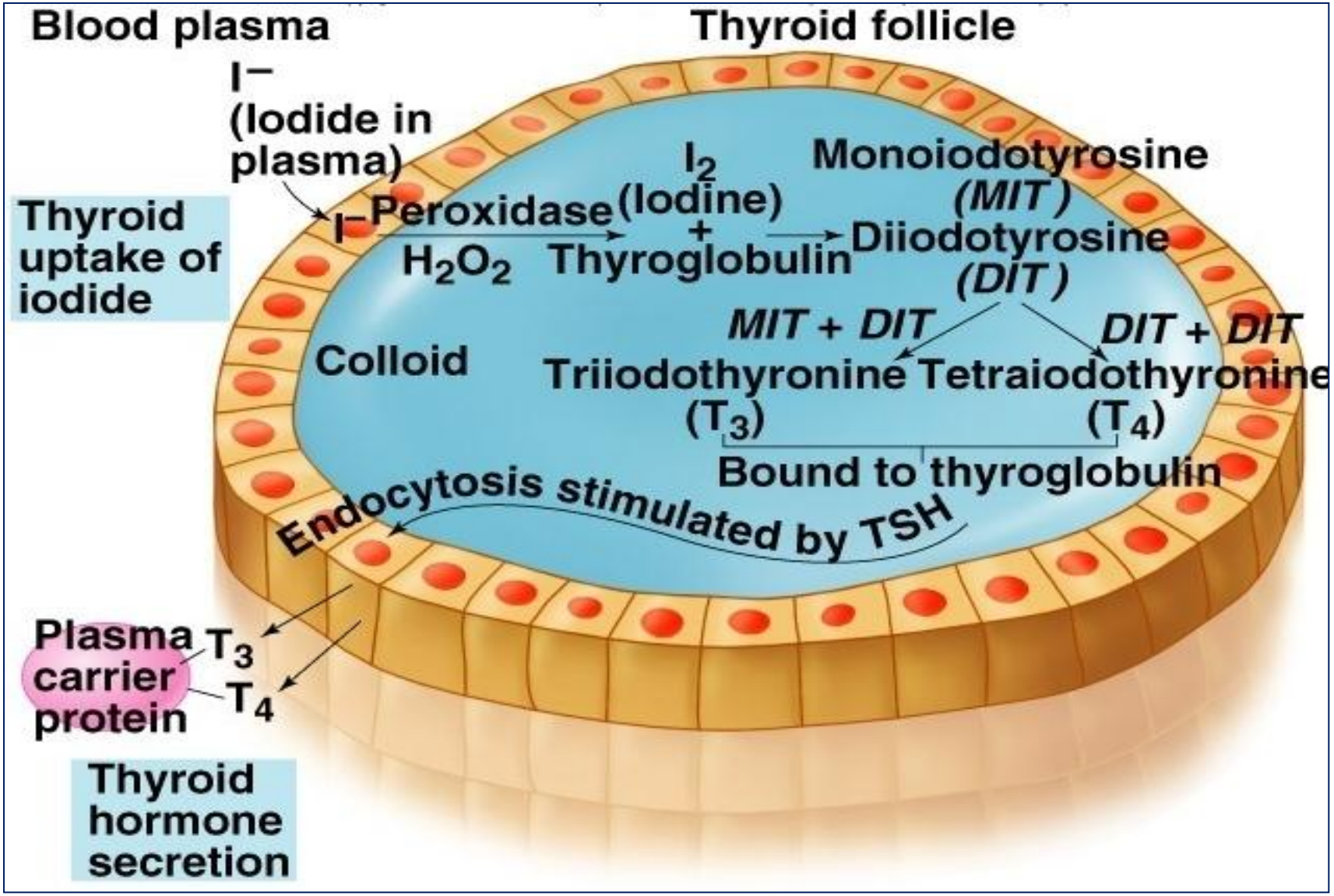
- **TSH** from anterior pituitary stimulates thyroid hormones (**T3,T4**) synthesis and secretion.
- **T3**and**T4** then stored in the follicles and released to the circulation by the effect of TSH.
- Because **iodine** is a component of T3and T4, an adequate amount of iodine in diet is required for thyroid hormones.
- The steps for synthesis of thyroid hormones include:
- **Iodide (I^-)** are taken up by thyroid follicle cells by active transport.
- **Thyroglobulins** which contain numerous **tyrosine** amino acid molecules are synthesized within the cells of the follicles.
- I^- is oxidized to **iodine I** by **peroxidase** .
- ***Either*** one iodine atom is bound to each tyrosine molecules of the thyroglobulin to form **monoiodotyrosine (MIT),**
- ***Or*** two of iodine atoms bound to tyrosine to form **diiodotyrosine .** This event occurs close to the time the thyroglobulin molecules are secreted by **exocytosis** into the lumen of the follicle.
- **I + TYROSINE ⟶ MIT**
- **Or: 2I + TYROSINE ⟶ DIT**

- In the lumen **two diiodotyrosine molecules** combine to form **T4,**

or **one monoiodotyrosine** and **one doiodotyrosine** combine to form **T3**.Large amounts of T3andT4 are stored within the thyroid follicles as part of thyroglobulin .

- Thyroglobulin is taken into the follicle cells by **endocytosis.**
- Thyroglobulin breaks down to **amino acids** and **T3andT4** by **proteolytic enzymes.**T3,T4 diffuse out of the follicle cells and enter the circulation. The remaining amino acids are used again to synthesize more thyroglobulin.

- **Pharmacology note**: Formation of **DIT** and **MIT** is called **organification,** which is inhibited by **thionamides propylthiouracil (PIU)** and **methimazole**, which are used to treat **hyperthyroidism**


Blood plasma
Thyroid follicle
I⁻
(Iodide in plasma)
Thyroid uptake of iodide
I⁻
Peroxidase
H2O2
I2
(Iodine)
+
Thyroglobulin
Monoiodotyrosine
(MIT)
Diiodotyrosine
(DIT)
MIT + DIT
DIT + DIT
Colloid
Triiodothyronine
(T3)
Tetraiodothyronine
(T4)
Bound to thyroglobulin
Endocytosis stimulated by TSH
Plasma carrier protein
T3
T4
Thyroid hormone secretion

- **Transport of T3, T4**
- 70-75% of circulating T3andT4 are bound to **thyroxin binding globulin (TBG**), which is synthesized by the liver.
- 20-30% of T3,T4 are bound to other plasma proteins **(Albumin).**
- 30-40% of T4 is converted to T3 in the body tissues.
- T3 is the major hormone that interacts with the target cells and is several times more potent than T4.
- Much of circulating T4 eliminated by conversion to **tetraiodothyroacetic acid**.

Physiological effects of T3, T4

- T3andT4 affect every tissues in the body but not in identical response:
- They regulate the metabolism at a normal metabolic rate:

- ⬆Thyroid hormones lead to ⬆ the basal metabolic rate.
- ⬆Thyroid hormones level lead to ⬆the rate of metabolism of protein, fat and glucose.
- Metabolic rate produces heat, causing **heat intolerance**.
- Blood level of cholesterol decline.
- Activity of $Na^+ – K^+$ pump which leads to body temperature.
- They can alter the number and activity of mitochondria to produce more ATP.
- They potentiate **catecholamine actions**.
- Thyroid hormones up regulate expression and stimulate activity of **β-adrenergic receptors** in the tissues such as heart and skeletal muscles causing enhanced sensitivity to circulating catecholamine.
- They act directly on the heart, stimulate contractility and increase the heart rate, result in high output **congestive heart failure.**
- In muscles, they contribute to **muscle tremors**

- **Regulation of thyroid hormones (T3, T4)**
- **TRH** released from the hypothalamus pass through the hypothalamohypophysial portal system to the anterior pituitary.
- Anterior pituitary secrete **TSH** which pass through the general circulation to the thyroid gland.
- **TSH** causes increased release of **T3**and**T4** from thyroid gland into general circulation.
- **T3**and **T4** act on target tissues to produce a response.
- T3 and T4 have an inhibitory effect on the secretion of TRH from the hypothalamus and TSH from the anterior pituitary.

Pathological conditions

- **Hyperthyroidism**
- It refers to a pathological **increase** in thyroid hormones synthesis.
- Manifestations of hyperthyroidism include:
- Weight loss with increased appetite.
- Heat intolerance.
- Diarrhea
- Often atrial fibrillation.
- T3andT4 concentrations are elevated in hyperthyroidism .TRH and TSH vary in concentration depending on the cause of hyperthyroidism.

Hypothyroidism

- It refers to decrease synthesis of thyroid hormones.
- Manifestation of hypothyroidism :
- Weight gain ,constipation
- Cold intolerance.
- Bradycardia and atrial fibrillation
- Dulled mentation.
- Congenital hypothyroidism may cause mental retardation **(cretinism**).
- T3, T4 are decreased, TRH, TSH concentration vary with the cause of hypothyroidism.
- **Euthyroid sick syndrome**
- Low to normal T3, T4 in ill patients with no appearance signs of thyroid dysfunction**.**

Calcitonin Hormone

- **Calcitonin** is secreted by the **parafollicular cells** of the thyroid gland.
- Increased level of Ca^{2+} in the blood leads to an increase secretion of calcitonin.
- The primary target tissue for calcitonin is the **bone**.
- Calcitonin causes decrease in **osteoclast** and lengthens the life span of **osteoblast** result in decrease in blood Ca^{2+} level and phosphate.
- Ca^{2+} level is regulated primarily by another hormone **(parathyroid hormone)** that is why complete **thyroidectomy** does not result in high blood Ca^{2+}.

THANKS