



Hormones

University Of Fallujah
College Of Medicine

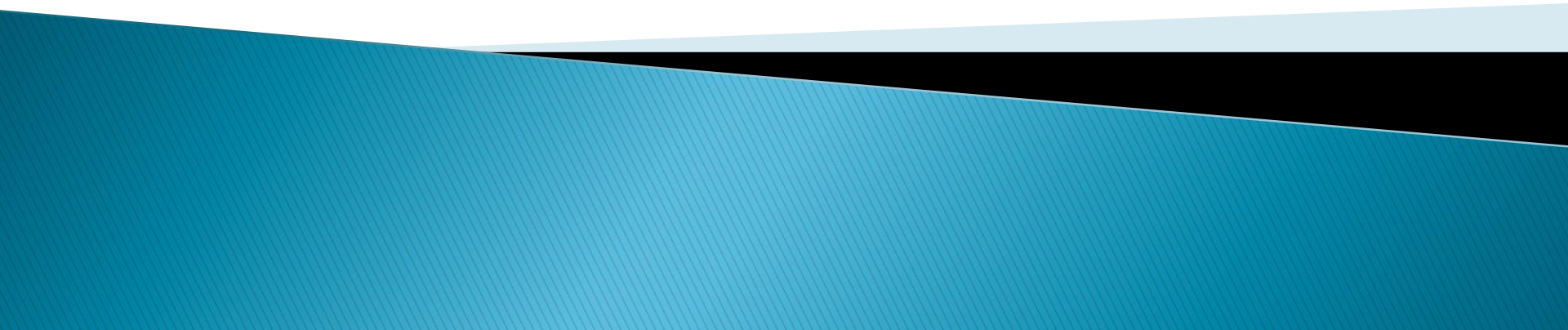
Lecture : (5)

Stage : 2th Stage

Lecturer : Dr. Mohammed amer

Department: Chemistry and Biochemistry

Biochemistry and Disorder of Hormones of the Thyroid Gland



□ Objectives:

1. To list the hormones synthesized by the thyroid gland and state their functions
2. To describe synthesis , regulation, and metabolism of thyroid hormones
3. To state the effects of increased and decreased Level of thyroid hormones on TSH Level .
4. To understand the disorders of the thyroid and the associated diseases such as :
 - ✓ **Hashimoto disease**
 - ✓ **Graves disease**
 - ✓ **Secondary hypothyroidism**
 - ✓ **Thyroid antibodies**

❑ **Thyroid Hormones & Metabolism**

- Secretes key metabolic hormones: Thyroxine (T4) and T3.
- Main Action: Stimulates oxidative respiration in most cells.
- Key Function: Sets and regulates the body's Basal Metabolic Rate (BMR).
- ❑ In children, these thyroid hormones also **promote growth** and stimulate **maturation of the central nervous system**.
- ❑ Children with an underactive thyroid gland experience stunted physical growth and severe mental impairment, a condition known as **cretinism**. This condition is distinct from pituitary dwarfism, which results from insufficient growth hormone (GH) production but does not affect intellectual development.

- ❑ People who are hypothyroid (**whose secretion of thyroxine is too low**) can take thyroxine orally, as pills.
- ❑ Only thyroxine and the steroid hormones (as in contraceptive pills), can be taken orally because they are nonpolar and can pass through the plasma membranes of intestinal epithelial cells without being digested.
- ❑ The thyroid gland also secretes **calcitonin**, a peptide hormone that plays a role in maintaining proper levels of calcium (Ca^{++}) in the blood. **When the blood Ca^{++} ↑ calcitonin stimulates the uptake of Ca^{++} into bones, thus lowering its level in the blood.**

1) **Thyroxin (T₄) and triiodotyronine T₃**

- Thyroid hormones are derivatives of the amino acid tyrosine bound covalently to iodine.
- The two principal thyroid hormones are:
 - ✓ **Thyroxine** (T₄ or L-3,5,3',5'-tetraiodothyronine)
 - ✓ **Triiodotyronine** (T₃ or L-3,5,3'-triiodothyronine).

- **Thyroid hormones are basically two tyrosines linked together with the critical addition of iodine at three or four positions on the aromatic rings.**

- ❑ **A large majority of the thyroid hormone secreted from the thyroid gland is T_4 , but T_3 is the considerably more active hormone.**
- ❑ Although a small amount of T_3 is directly secreted, the majority is produced through deiodination of T_4 in peripheral tissues, particularly in the liver and kidneys.
- ❑ This process also generates reverse T_3 (r T_3), a biologically inactive form with no known metabolic function..
- ❑ Thyroid hormones are poorly soluble in water, and more than 99% of the T_3 and T_4 circulating in blood is bound to carrier proteins. The principle carrier of thyroid hormones is **thyroxine-binding globulin**, a glycoprotein synthesized in the liver.

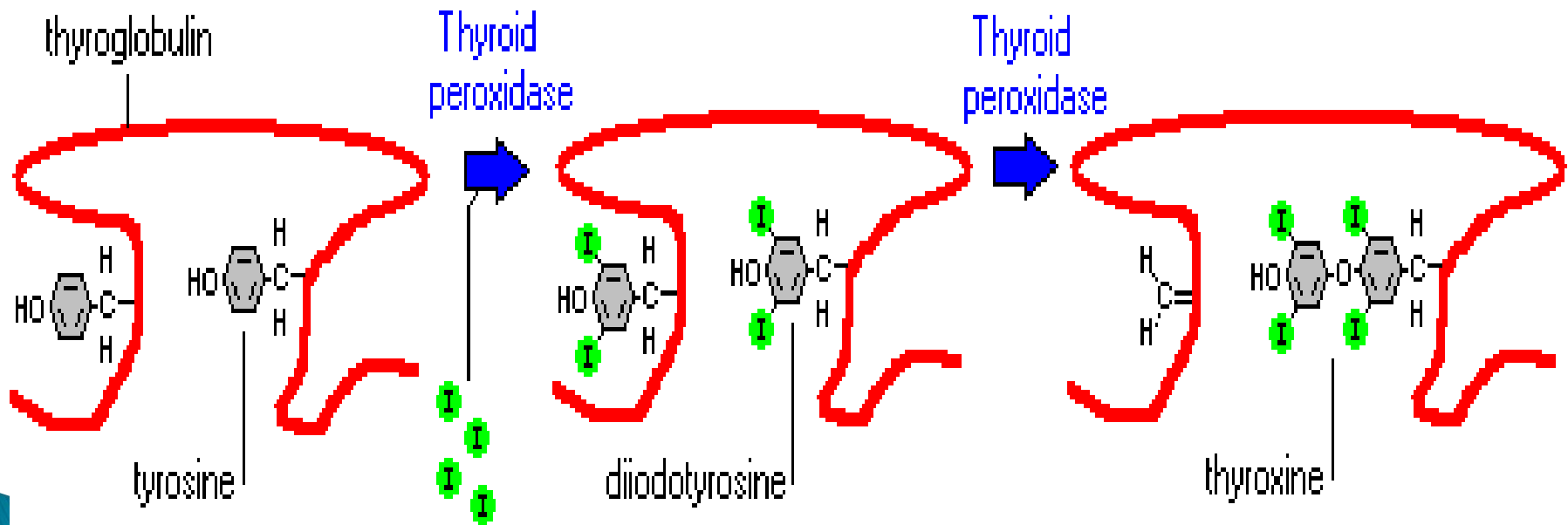
❑ **Synthesis and Secretion of Thyroid Hormones**

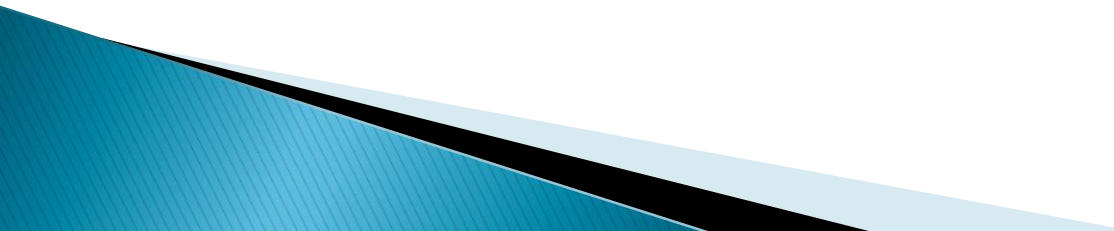
- The entire synthetic process occurs in three major steps:
- ✓ Production and accumulation of the raw materials
- ✓ Fabrication or synthesis of the hormones on a backbone or scaffold of precursor
- ✓ Release of the free hormones from the scaffold and secretion into blood

❑ **Raw materials:**

- **Tyrosines** are provided from a large glycoprotein scaffold called **thyroglobulin**,. A molecule of thyroglobulin contains 134 tyrosines, although only a handful of these are actually used to synthesize T_4 and T_3 .
- **Iodine**, or more accurately iodide (I^-), is taken up from blood by thyroid epithelial cells, which have on their outer plasma membrane an "*iodine trap*". Once inside the cell, iodide is transported into the lumen of the follicle along with thyroglobulin.

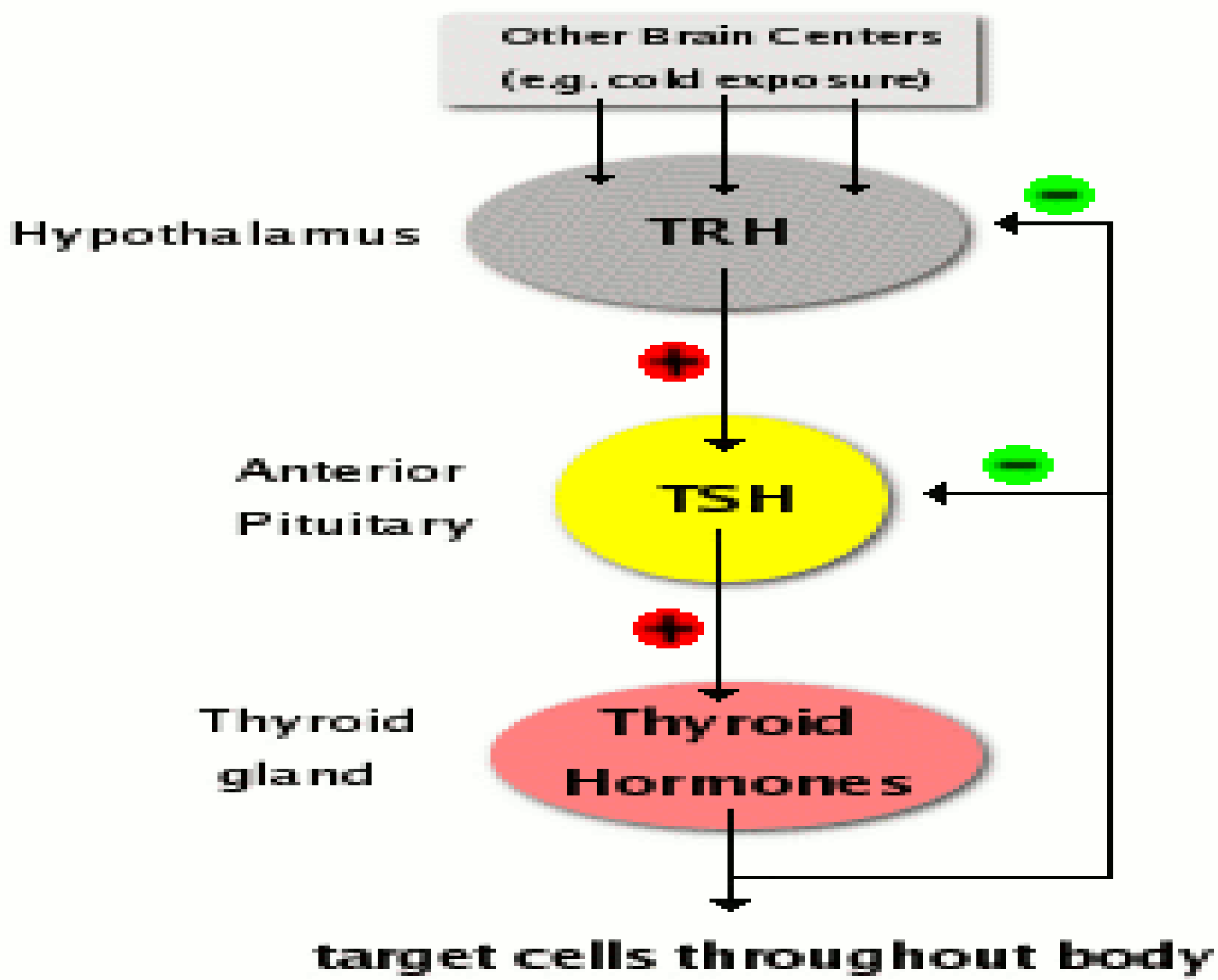
- ❑ **Fabrication of thyroid hormones is conducted by the enzyme thyroid peroxidase,**
- ✓ Thyroid peroxidase catalyzes two sequential reactions:
 1. Iodination of tyrosines on thyroglobulin (also known as "organification of iodide").
 2. Synthesis of thyroxine or triiodothyronine from two iodotyrosines.



- ❑ **Thyroid hormones are released from the thyroglobulin scaffold through proteolytic digestion within the lysosomes of the thyroid follicular (epithelial) cells .**
 - Free thyroid hormones diffuse from the lysosomes across the basolateral plasma membrane of the thyroid epithelial cell into the circulation, where they rapidly bind to plasma carrier proteins for transport to their target tissues.
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❑ **Control of Thyroid Hormone Synthesis and Secretion**

- ✓ Each of the processes described above appears to be stimulated by thyroid-stimulating hormone from the anterior pituitary gland.
- ✓ Binding of TSH to its receptors on thyroid epithelial cells stimulates synthesis of the iodine transporter, **thyroid peroxidase and thyroglobulin**.
- ✓ When TSH levels are low, rates of thyroid hormone synthesis and release diminish.
- ✓ The thyroid gland is part of the hypothalamic- pituitary- thyroid axis, and control of thyroid hormone secretion is exerted by classical negative feedback.



❑ **Thyroid Hormone Receptors and Mechanism of Action**

- Receptors for thyroid hormones are intracellular DNA-binding proteins that function as hormone-responsive transcription factors, very similar conceptually to the receptors for steroid hormones.

❑ **Metabolic Effects of Thyroid Hormones**

- ✓ Thyroid hormones have profound effects on many physiologic processes, such as development, growth and metabolism.
- ✓ They stimulate diverse metabolic activities most tissues, leading to an **increase in basal metabolic rate**.
- ✓ One consequence of this activity is to **increase body heat production**, which seems to result, at least in part, from increased oxygen consumption and rates of ATP hydrolysis.
- ✓ A few examples of specific metabolic effects of thyroid hormones include:

- 1) **Lipid metabolism:** Increased thyroid hormone levels stimulate fat mobilization, leading to increased concentrations of fatty acids in plasma.
- 2) **Carbohydrate metabolism:** Thyroid hormones stimulate almost all aspects of carbohydrate metabolism, including enhancement of insulin-dependent entry of glucose into cells and increased gluconeogenesis and glycogenolysis to generate free glucose.

❑ **Other Effects: A few additional, effects of thyroid hormones include:**

- A. **On muscle:** T₃ increases glucose uptake by muscle cells it also stimulate protein synthesis and therefore growth of muscle through its stimulatory actions on gene expression. Glycolysis in muscle is increased by this action of T₃.

- B. **On the pancreas:** thyroid hormone increases the sensitivity of the β cells of the pancreas to those stimuli that normally promote insulin release and is required for optimal insulin secretion
- C. **On Cardiovascular system:** Thyroid hormones increases heart rate, cardiac contractility and cardiac output.
- D. **On Central nervous system:** Both decreased and increased concentrations of thyroid hormones lead to alterations in mental state.
- E. **On Reproductive system:** Normal reproductive behavior and physiology is dependent on having essentially normal levels of thyroid hormone. Hypothyroidism in particular is commonly associated with infertility.

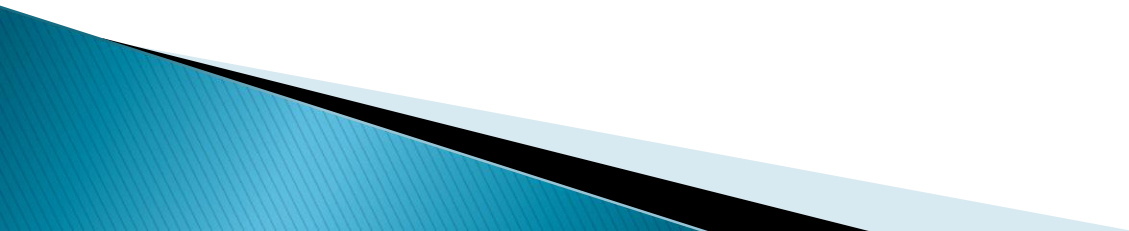
□ Thyroid Disease States

1. **Hypothyroidism** : a deficiency in thyroid hormone secretion and action
 - a. **Primary**: the synthesis of T4 and T3 is impaired due to one or more of the following:
 - i. Iodine deficiency
 - ii. Infiltrative disease the thyroid as (Hashimoto's disease)
 - iii. Defects in the thyroid hormone synthesis (thyroidectomy)
 - iv. Enzyme defect .
 - v. Atrophic hypothyroidism (DM, Addison)
 - vi. Drugs and drug that (low absorption as iron , omeprazole.
 - b. **Secondary**: (central) occurs as a result of pituitary or hypothalamic disease that produce a deficiency in TSH, TRH or both.

2. **Hyperthyroidism (thyrotoxicosis):** a hyper-metabolic condition caused by excessive production of thyroid hormones. Causes are divided into:

- a. Those that are associated with clinically evident hyperthyroidism and increased production and secretion of thyroid hormones from the gland:
 - i. . Graves's disease: development of IgG antibody against the thyroid TSH receptor resulting n overproduction of T4 and T3.
 - ii. Autonomous production by thyroid nodules
 - iii. A toxic solitary edema
 - iv. Excessive TSH secretion (rare)
- b. *Those that are not*
 - i. Exogenous intake
 - ii. Iodine ingestion in excess
 - iii. Thyroid carcinoma
 - iv. Drug induced thyrotoxicosis with iodine containing medication

Euthyroid sick syndrome (Homework)



Good luck ▶