

# Endocrine System

## Thyroid Gland

Assistant Professor Dr.Qayssar Joudah Fadheel

Ph.D. Pharmacology & Therapeutics

Head of Department of Pharmacology & Toxicology

College of Pharmacy / University of Babylon

# THYROID HORMONES

- The thyroid gland help normal growth and maturation by **maintaining a level of metabolism in the tissues that is optimal for their normal function.**
- The two major thyroid hormones are
- **tri-iodothyronine (T3; the most active form)**
- and **thyroxine (T4).**

# THYROID HORMONES

- Although the thyroid gland is not essential for life, inadequate secretion of thyroid hormone (**hypothyroidism**) results in bradycardia, poor resistance to cold, and mental and physical slowing (in children, this can cause mental retardation and dwarfism).
- If an excess of thyroid hormones is secreted (**hyperthyroidism**) result in tachycardia and cardiac arrhythmias, body wasting, nervousness, tremor, and excess heat production can occur.

# Thyroid hormone synthesis and secretion

- Thyroid function is controlled by a thyroid-stimulating hormone (TSH; thyrotropin).
- Secretion of TSH by the anterior pituitary is stimulated by hypothalamic TRH.
- TSH action is mediated by CAMP and leads to stimulation of iodide ( $I^-$ ) uptake.
- Oxidation to iodine ( $I_2$ ) by a peroxidase is followed by iodination of tyrosine on thyroglobulin.

# Thyroid hormone synthesis and secretion

- Condensation of two diiodotyrosine residues gives rise to T<sub>4</sub>, whereas condensation of a monoiodotyrosine residue with a diiodotyrosine residue generates T<sub>3</sub>, which is still bound to the protein.
- Most of the hormone (T<sub>3</sub> and T<sub>4</sub>) is bound to thyroxine-binding globulin in the plasma.

- **Mechanism of action :**
- Both **T4** and **T3** must dissociate from thyroxine-binding plasma proteins prior to entry into cells, either by diffusion or by active transport.
- In the cell, **T4** is enzymatically deiodinated to **T3**, which enters the nucleus and attaches to specific receptors.
- The activation of these receptors promotes the formation of RNA and subsequent protein synthesis, which is responsible for the effects of **T4**.

- **Pharmacokinetics**

- Both **T4** and **T3** are absorbed after oral administration.
- Food, calcium preparations, and aluminum-containing antacids can decrease the absorption of T4 but not of T3.
- The hormones are metabolized through the microsomal P450 system.
- Drugs that induce the P450 enzymes, such as phenytoin, rifampin, and phenobarbital, accelerate metabolism of the thyroid hormones .

# Treatment of hypothyroidism

- Hypothyroidism usually results from autoimmune destruction of the gland and is diagnosed by elevated TSH.
- It is treated with levothyroxine (T4) .
- The drug is given once daily because of its long half-life.
- Steady state is achieved in 6 to 8 weeks.
- **Toxicity** is directly related to T4 levels and marked itself as nervousness, heart palpitations and tachycardia, intolerance to heat, and unexplained weight loss.



# Treatment of hyperthyroidism (Thyrotoxicosis)

Excessive amounts of thyroid hormones in the circulation are associated with a number of disease states, including Graves disease, toxic adenoma, and goiter.

- In these situations, TSH levels are reduced due to negative feedback.
- The goal of therapy is to decrease synthesis and/or release of additional hormone.
- This can be accomplished by:

- **1- Inhibition of thyroid hormone synthesis:**
- **The thioamides, propylthiouracil (PTU) and methimazole,**
- **Carbimazole** (which is converted into methimazole in the body) are concentrated in the thyroid, where they inhibit both the oxidative processes required for iodination of tyrosyl groups and the condensation (coupling) of iodotyrosines to form T3 and T4.
- **PTU** can also block the conversion of T4 to T3 .
- The thioamides are well absorbed from the gastrointestinal tract, but they have short half-lives.
- Several doses of PTU are required per day.
- Methimazole is administered in 3 equally divided doses at approximately 8-hour intervals.
- Relapse may occur.

- **Adverse effects** : are rare include agranulocytosis (severe decrease in the production of white blood cells) , rash, and oedema .
- Because of the potential for liver toxicity or liver failure PTU should be reserved only for patients who are intolerant of methimazole.
- There are three other very rare complications of antithyroid drugs: **liver damage** (more common with propylthiouracil), **aplastic anemia** (failure of the bone marrow to produce blood cells), and **vasculitis** (inflammation of blood vessels associated with propylthiouracil).

- Propylthiouracil used to be the drug of choice during **pregnancy** because it causes less severe birth defects than methimazole.
- But experts now recommend that propylthiouracil be given during the first trimester only.
- This is because there have been rare cases of liver damage in people taking propylthiouracil.
- After the first trimester, women should switch to methimazole for the rest of the pregnancy.
- For women who are nursing, methimazole is probably a better choice than propylthiouracil (to avoid liver side effects).

## **2. Removal of part or all of the thyroid gland:**

This can be done either by surgery or by destruction of the gland by beta particles emitted by **radioactive iodine ( $I_{131}$ )**, which is selectively taken up by the thyroid follicular cells.

- Younger patients are treated with the isotope without prior pre-treatment with methimazole whereas the opposite is the case in elderly patients.
- Most patients become hypothyroid as a result of this drug and require treatment with levothyroxine.

- **3. Blockade of hormone release:**
- A pharmacologic dose of **iodide** inhibits the iodination of tyrosines, but this effect lasts only a few days.
- **Iodide** inhibits the release of thyroid hormones from thyroglobulin.
- It is employed to treat potentially fatal thyrotoxic crisis (thyroid storm) or prior to surgery, because it decreases the vascularity of the thyroid gland.
- It is not useful for long-term therapy, because the thyroid ceases to respond to the drug after a few weeks.
- It is administered orally.
- **Adverse effects** are relatively minor and include sore mouth and throat, swelling of the tongue or larynx, rashes, ulcerations of mucous membranes, and a metallic taste in the mouth.

**4. Thyroid storm** : Thyroid storm presents with extreme symptoms of hyperthyroidism.

- The therapeutic options for thyroid storm are the same as those for hyperthyroidism, except that the drugs are given in higher doses and more frequently.
- **$\beta$ -Blockers** that lack sympathomimetic activity, such as *propranolol*, are effective for sympathetic stimulation that occurs in hyperthyroidism.
- Intravenous administration is effective in treating thyroid storm.
- An alternative in patients suffering from severe heart failure or asthma is the **calcium-channel blocker ( diltiazem )**
- Other agents used in the treatment of thyroid storm include PTU, iodides, iodinated contrast media (which rapidly inhibits the conversion of T4 to T3) and glucocorticoids (to protect against shock).

Thank You