

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

السلام عليكم ورحمة الله وبركاته

Al-Mustaqbal University College
Pathophysiology
3rd stage

Endocrine introduction
And
Disorders of thyroid function

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The Endocrine System

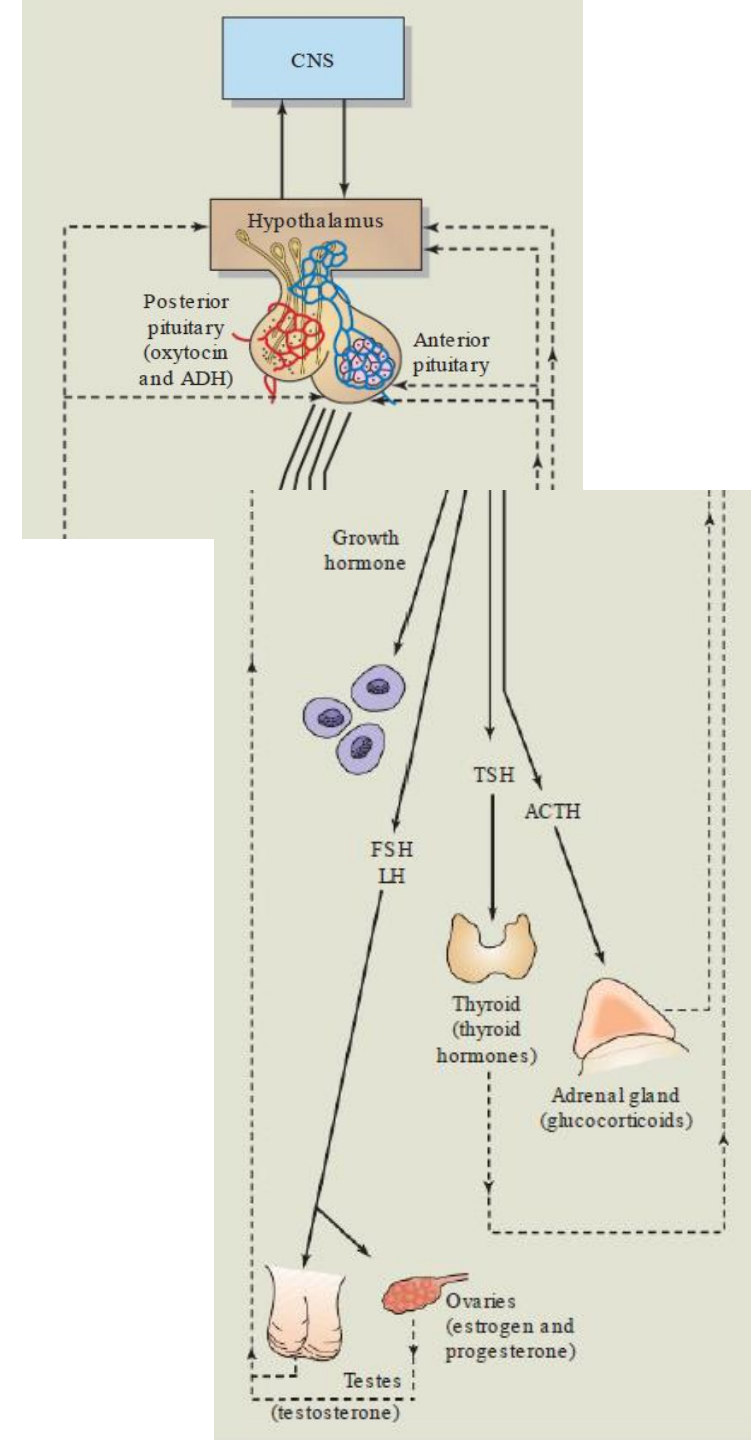
The endocrine system, along with the nervous system, allows for communication between distant sites in the body.

There are three components to the endocrine system:

- 1- Endocrine glands.
- 2- Hormones.
- 3- Target cells or organs that respond to the hormones.

Endocrine Glands

Endocrine glands are organs that synthesize, store, and secrete hormones into the bloodstream.



Hormones

A hormone is a chemical messenger released by an endocrine gland into the circulation.

Once released, a hormone travels in the bloodstream and affects only cells (target cells) in the body that have **receptors (binding sites)** specific to it.

Typically, a hormone is released in a pattern that often follows an inherent **daily (diurnal) rhythm**.

Amine hormone

The amine hormones are derivatives of the amino acid tyrosine and include thyroid hormone and the catecholamines (epinephrine, norepinephrine, and dopamine).

Peptide Hormones

Peptide hormones range in size from a few amino acids to relatively large protein complexes.

Peptide hormones circulate in the plasma to their target organs and exert their effects by binding to specific receptors present on the outside of target cell membranes.

e.g. hormones of hypothalamic-pituitary hormonal system

Steroid Hormones

Steroid hormones are cholesterol-based, lipid-soluble molecules produced by the adrenal cortex and the sex organs. Because steroid hormones are lipid-soluble, they can cross the cell membrane and bind to receptors or carriers inside the cell.

e.g. **Estrogens**

Progesterone

Androgens (primarily testosterone)

Aldosterone

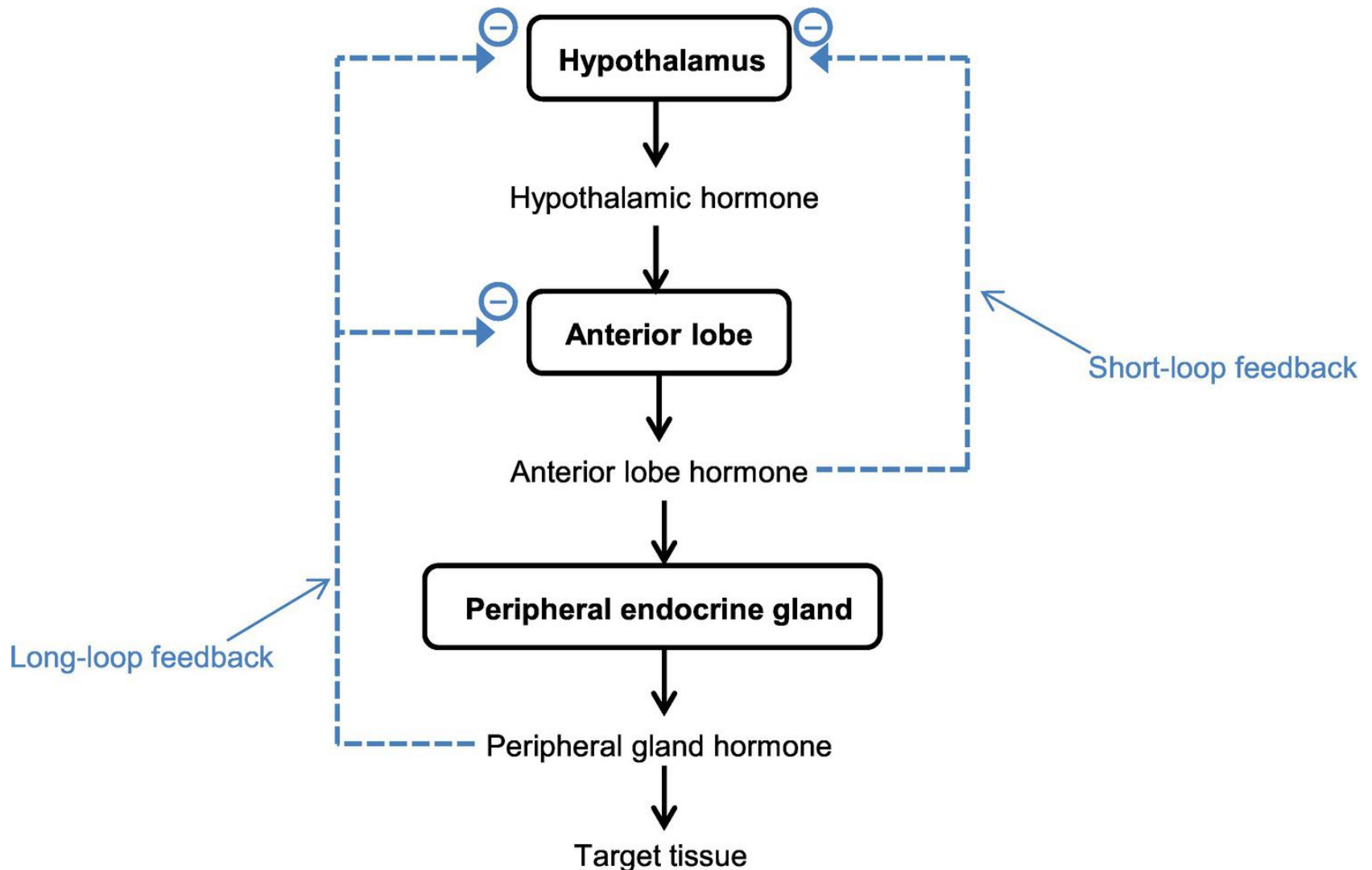
Glucocorticoids

Target Glands

The third group of endocrine glands are outside the brain that respond to the anterior and posterior pituitary hormones with the release of their own hormones. These glands are the target organs of the pituitary hormones and include the thyroid gland, the adrenal gland, the testes and ovaries, and the pancreas, which secretes insulin, is also an endocrine gland.

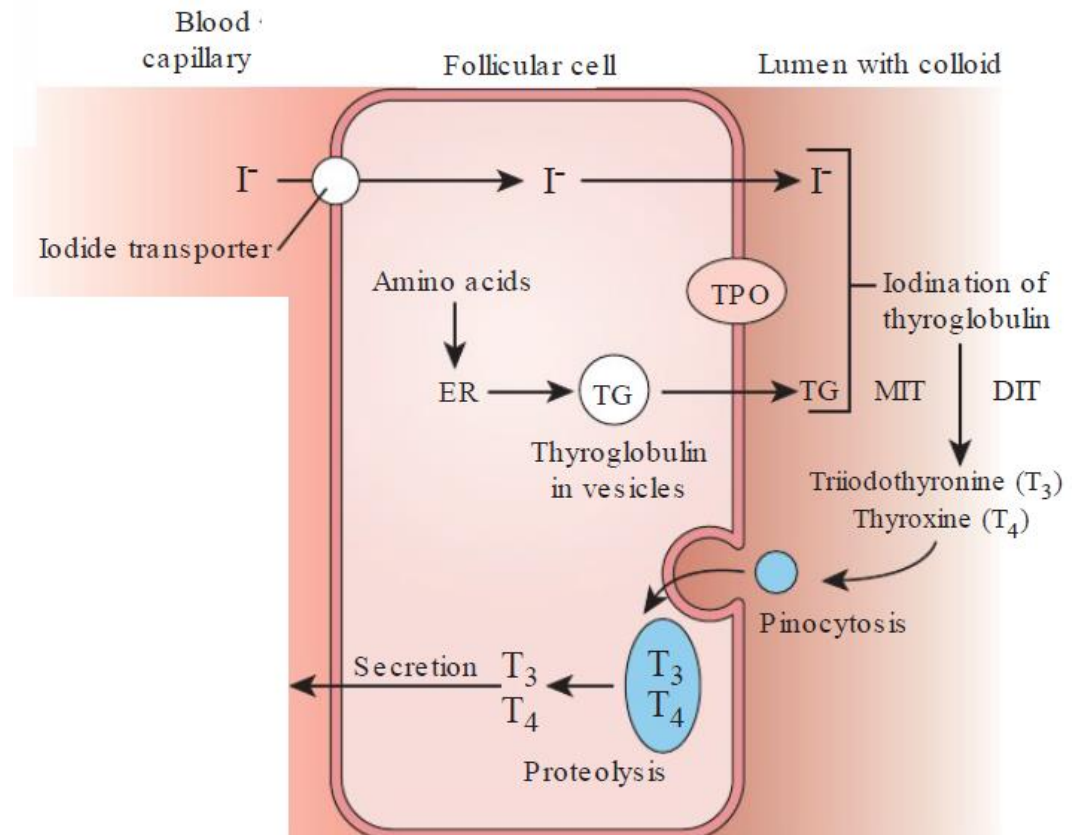
Feedback mechanism of endocrine system

In the endocrine system, feedback refers to the response of a target tissue after stimulation by a specific hormone that then influences the continued release of that hormone.



Thyroid Hormone

Thyroid hormone (TH) is an amine hormone synthesized and released from the thyroid gland. It is made when one or two iodine molecules are joined to a large glycoprotein called thyroglobulin, which is synthesized in the thyroid gland and contains the amino acid tyrosine. These iodine-containing complexes are called iodotyrosines. Two iodotyrosines then combine to form two types of circulating TH, called T_3 and T_4 .



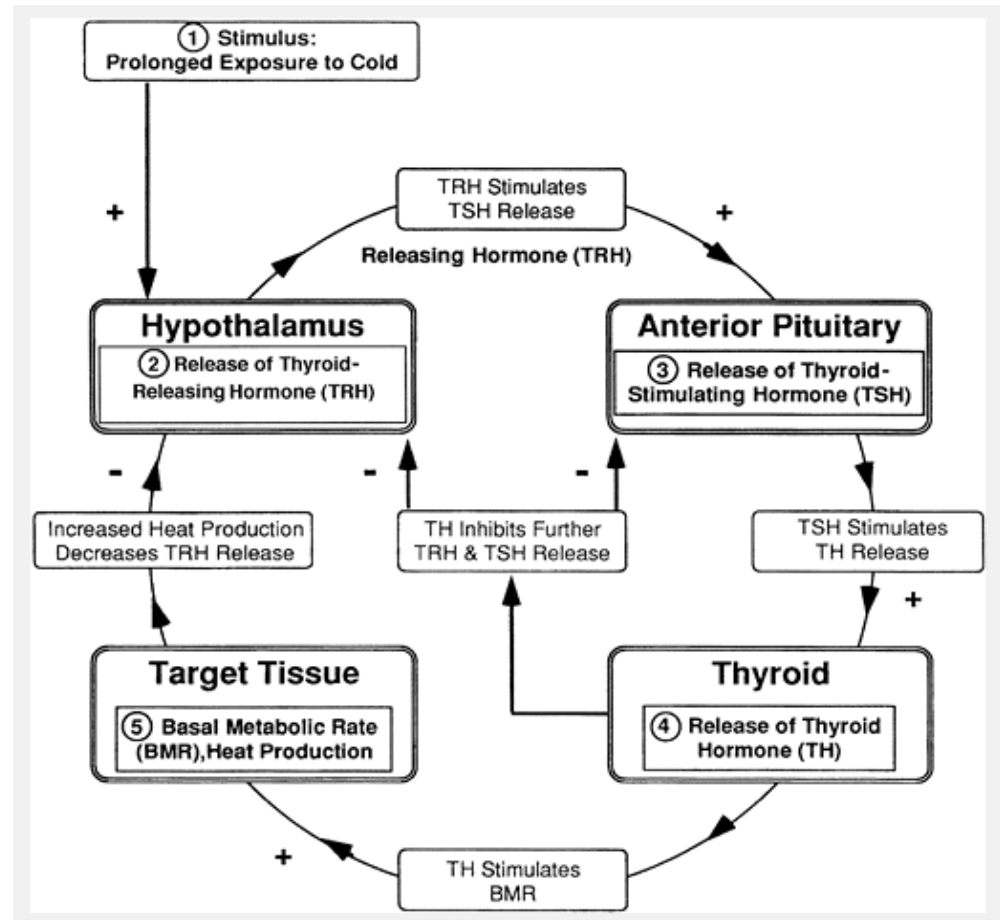
Effects of Thyroid Hormone

Target cells for TH include almost all cells of the body. The primary effect of TH is to stimulate the metabolic rate of all target cells by increasing the metabolism of protein, fat, and carbohydrate.

The stimuli responsible for increasing TRH secretion include exposure of the body to:

cold temperature, physical and perhaps psychological stress, and low levels of TH.

When the secretion of TRH is stimulated by cold temperature, the result is an increase in TH, which **increases basal metabolic rate**.



Effects of Thyroid Hormone

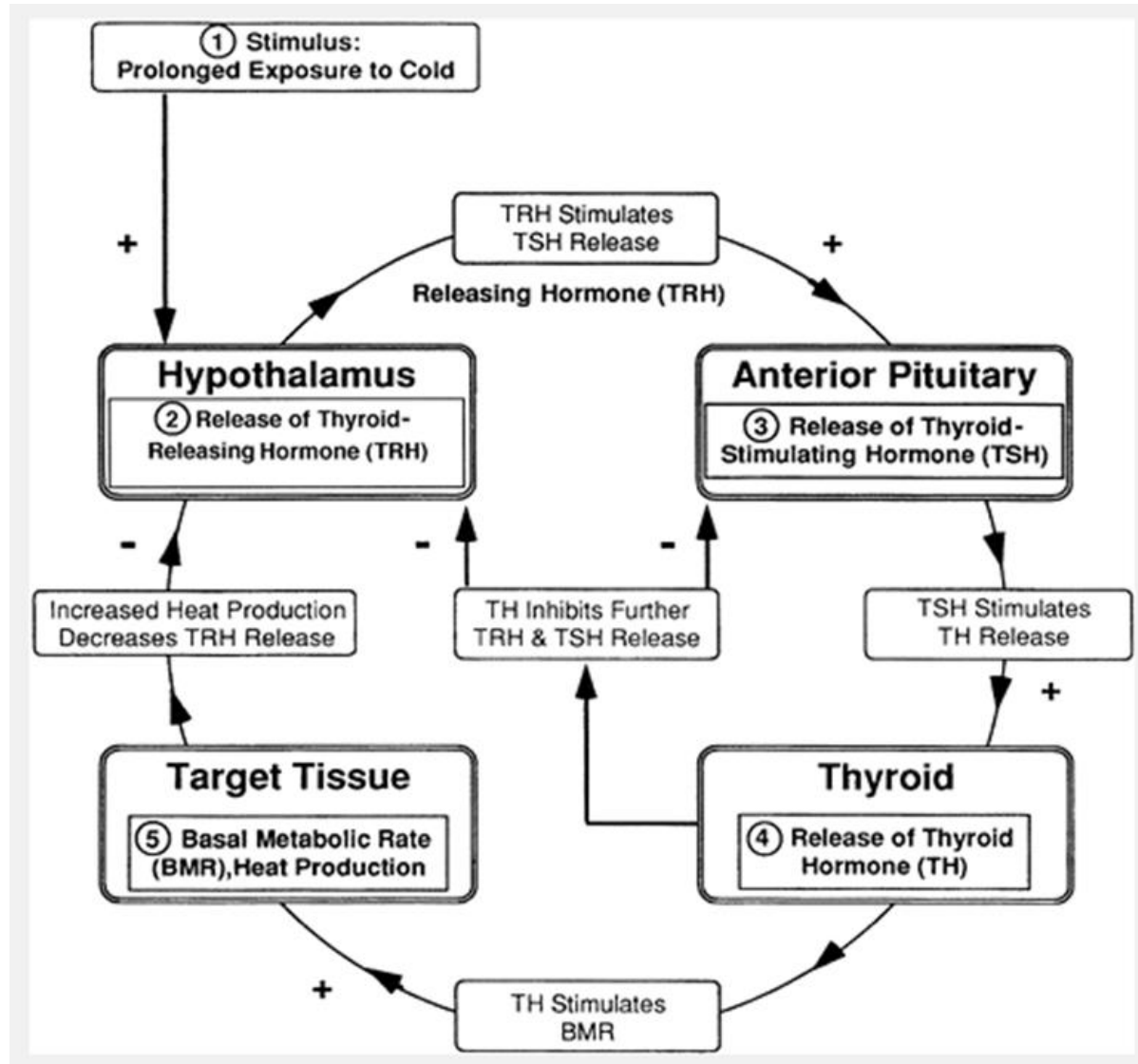
The thyroid hormone is essential to:

- 1- Normal body **growth** in infancy and childhood.
- 2- **Controlling body temperature.**
- 3- **Regulating protein, fat and carbohydrate catabolism in all cells.**
- 4- It keeps up **growth hormone release, skeletal maturation, and heart rate ,force and output.**
- 5- It promotes **central nervous system growth.**
- 6- Stimulate **synthesis of many enzymes.**
- 7- Thyroid is necessary for **muscle tone and vigor.**

Disorders of thyroid function

Hypothyroidism

Hypothyroidism results from decreased levels of circulating thyroid hormone.



Disorders of thyroid function

Hypothyroidism

Hypothyroidism results from decreased levels of circulating thyroid hormone.

Hypothyroidism may result from malfunction of the thyroid gland, the pituitary, or the hypothalamus.

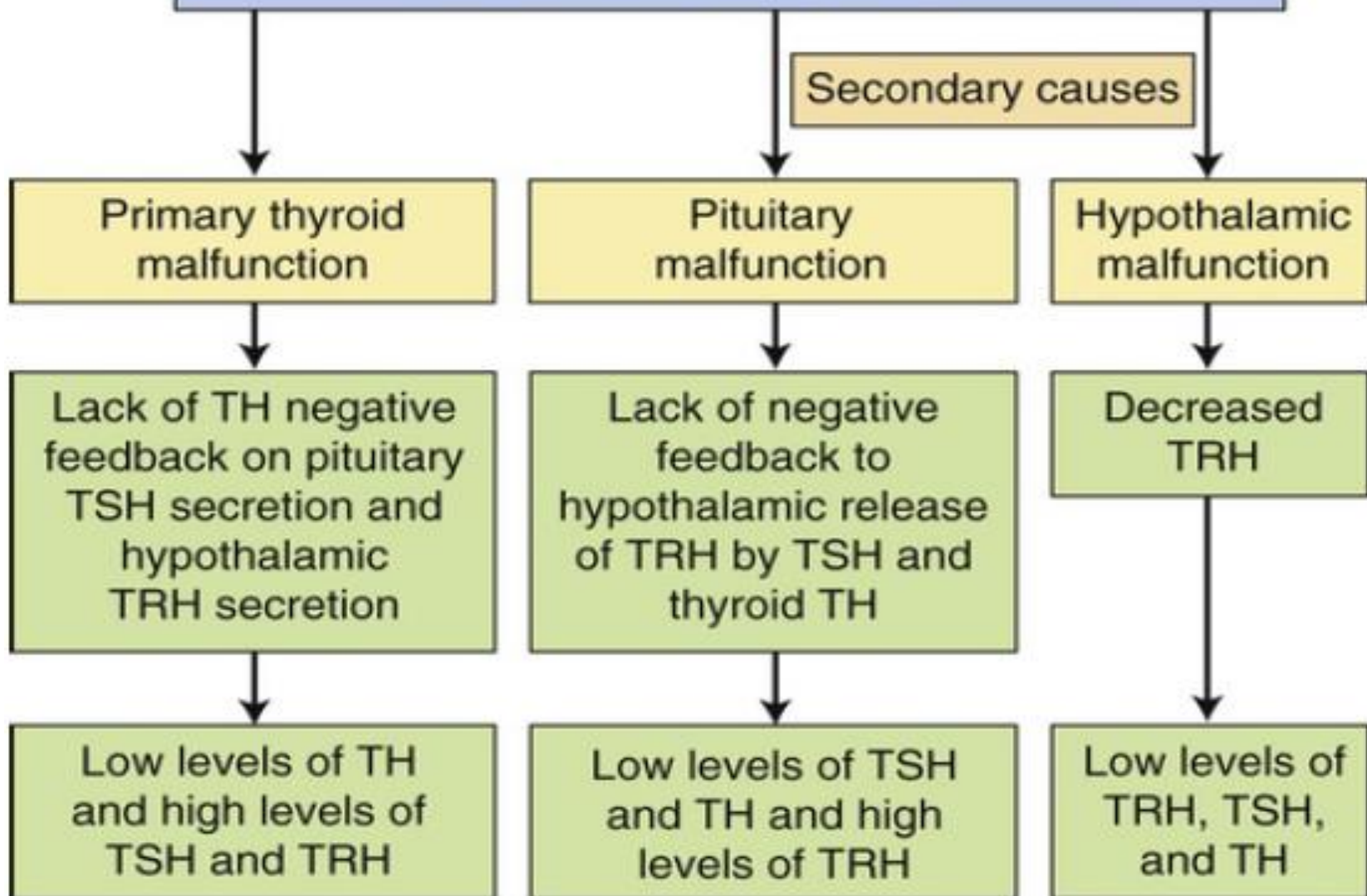
If it results from thyroid gland malfunction, low TH levels are accompanied by high TSH and high TRH because of the lack of negative feedback on the pituitary and hypothalamus by TH.

If hypothyroidism results from pituitary malfunction, low levels of TH are caused by low TSH. TRH from the hypothalamus is high because there is no negative feedback on its release by TSH or TH.

Hypothyroidism caused by hypothalamic malfunction results in low TH, low TSH, and low TRH.

Medically-induced hypothyroidism may follow previous thyroid therapy or surgery, radioiodine therapy, or drugs such as cytokines, amiodarone, and lithium.

Mechanisms of hypothyroidism

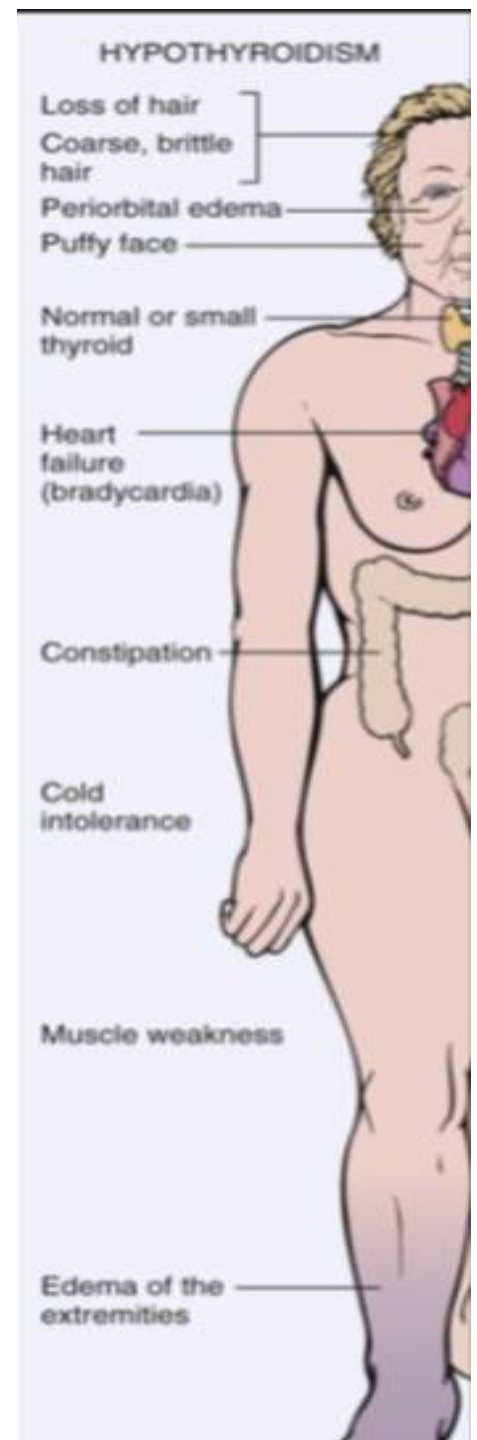


Diseases of Hypothyroidism

- Hashimoto's disease, also called **autoimmune thyroiditis**, results from **autoantibody destruction of thyroid gland tissue**. This results in decreased TH, with increased TSH and TRH levels caused by minimal negative feedback. The cause of autoimmune thyroiditis is unknown, but there appears to be a genetic tendency to develop the disease.
- Endemic goiter is hypothyroidism caused by a **dietary deficiency** of iodide. A goiter is an enlargement of the thyroid gland. Goiter occurs with a deficiency of iodide because the thyroid cells become **overactive and hypertrophic (larger)** in an attempt to sequester all possible iodide from the bloodstream. **Low TH** levels are accompanied by high **TSH and TRH** because negative feedback is minimal.
- **Thyroid carcinoma may cause hypothyroidism or hyperthyroidism**. Treatment of this rare cancer may include thyroidectomy, TSH suppression drugs, or radioactive iodine therapy to destroy thyroid tissue. All of these treatments may result in **hypothyroidism**.

Clinical Manifestations

- Sluggishness, slow thinking, slow movements.
- Decreased heart rate and cardiac output, enlarged heart.
- Edema of the skin.
- Intolerance to cold temperatures.
- Decreased metabolic rate, decreased caloric requirements, decreased appetite and nutrient absorption across the gut.
- Constipation.
- Change in reproductive function.
- Dry, flaky skin and brittle, thin body and head hair.



Diagnosis: early change is T3 & T4 ↓ , TSH ↑, subclinical hypothyroidism. Show normal T3 & T4 , TSH ↑, & should be treated early before complications start .

Treatment

- Treatment always includes replacement of thyroid hormone with synthetic thyroxine.
- For endemic goiter, iodide replacement may relieve symptoms.
- If the cause of hypothyroidism is related to a central nervous system tumor, it may be treated with chemotherapy, radiation, or surgery.

Thyrotoxicosis

Thyrotoxicosis is a condition that results from any cause of increased TH levels.

Hyperthyroidism is a form of thyrotoxicosis in which excess amounts of TH are secreted from the thyroid gland.

Hyperthyroidism include Graves disease, toxic multinodular goiter. Thyrotoxicosis not associated with hyperthyroidism like ingestion of excessive TH.

Hyperthyroidism

Hyperthyroidism is excessive levels of circulating TH. This disorder can result from dysfunction of the thyroid gland, pituitary, or hypothalamus. Increased TH caused by malfunction of the thyroid gland is accompanied by decreased TSH and TRF, as a result of the negative feedback on their release by TH.

Diseases of Hyperthyroidism

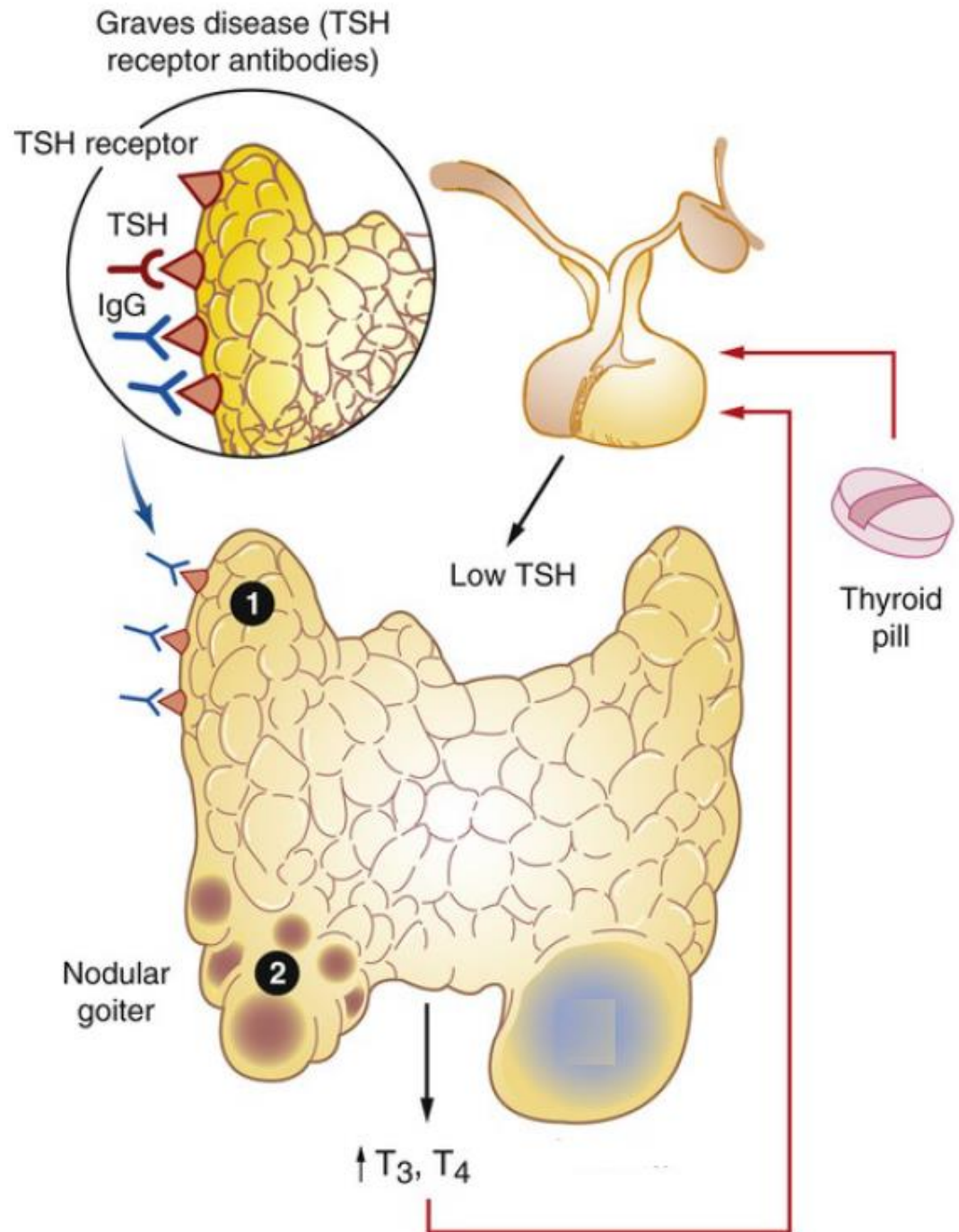
Graves' disease, the most common cause of hyperthyroidism, is an **autoimmune disorder** usually characterized by production of **autoantibodies that mimic the action of TSH on the thyroid gland**.

The cause of Graves' disease is unknown; however, there appears to be a genetic predisposition to autoimmune disease.

Women in their **20s and 30s** are most often diagnosed, although the disease may start during the teen years.

These IgG autoantibodies, termed thyroid-stimulating immunoglobulins, turn on the production of TH, but are not inhibited by rising levels.

TSH and TRH levels are low because they are inhibited by high TH.



Nodular goiter

Nodular goiter is an **increase in the size of the thyroid gland** caused by **increased demand** for thyroid hormone.

Increased demand for thyroid hormone occurs during periods of growth or excess metabolic demand such as puberty or pregnancy.

In these cases, increased TH is caused by metabolically driven activation of the hypothalamus, and therefore is accompanied by increased TRH and TSH.

When the demand for thyroid hormone is **lessened**, the thyroid **gland usually returns** to its previous size.

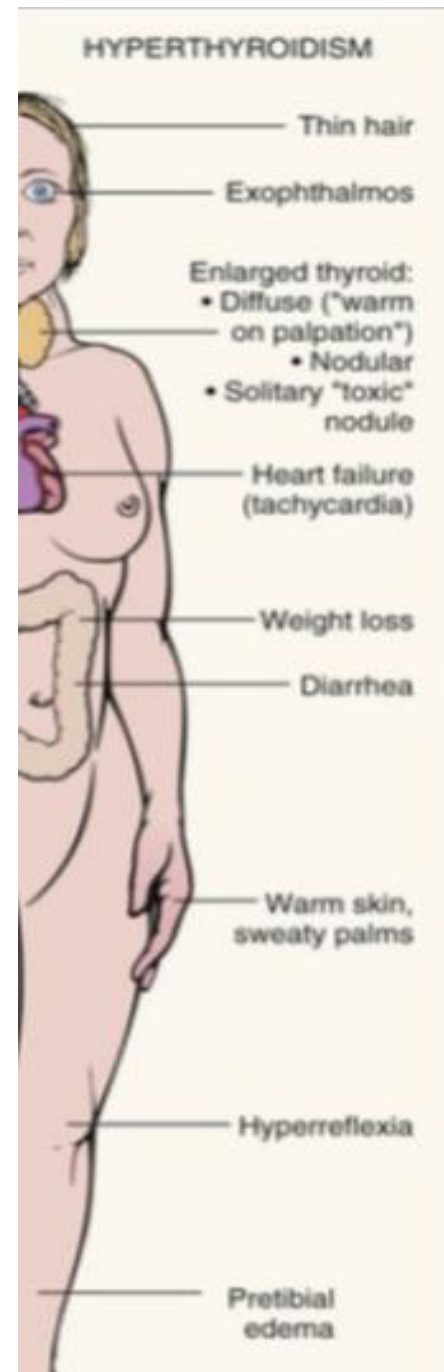
Occasionally, **irreversible changes** may have occurred and the gland does not regress.

The enlarged thyroid may continue to produce **excess TH**. If the individual remains hyperthyroid, the condition is referred to as a **toxic nodular goiter**.

Clinical Manifestations

The clinical features of thyrotoxicosis are attributable to the metabolic effects of increased circulating levels of thyroid hormones.

- Increased heart rate.
- Increased muscle tone, tremors, irritability, increased sensitivity to catecholamines.
- Increased basal metabolic rate and heat production, intolerance to heat, excess sweating.
- Weight loss, increased hunger.
- A staring appearance.
- Exophthalmos (bulging of the eyes) may develop.
- Increased number of bowel movements.
- Goiter (usually), which is an increase in the size of the thyroid gland.
- Changes in skin and hair condition may occur.
- Reproductive irregularities.



- **Diagnostic Tools**

- A good history and physical examination will help diagnose hyperthyroidism.
- **Blood tests measuring levels of TH: T3 & T4 ↑ , TSH ↓ .**

In **subclinical** hyperthyroidism, **T3 & T4 normal** , **TSH ↓** this indicate early disease & the best time for treatment.

- Decreased serum lipids may accompany hyperthyroidism.
- Decreased sensitivity to insulin, which may result in hyperglycemia.
- **Isotope scan:** diffuse uptake in **Gravis disease**.
- **US:** for enlargement nodules.

Complications

- Arrhythmias are common in patients with hyperthyroidism and may be the presenting symptom of the disorder.

Any person complaining of arrhythmia should be evaluated for thyroid disorder.

- A life-threatening complication of hyperthyroidism is thyrotoxic crisis (thyroid storm).

Treatment

Treatment depends on the site and cause of hyperthyroidism.

- If the problem is at the level of the thyroid gland, treatment usually involves **anti-thyroid drugs** that block TH production or/and **beta-blocking** drugs to decrease sympathetic hyper-responsiveness.
- Drugs that destroy thyroid tissue also may be used. For instance, **radioactive iodine (I^{131})** administered in oral form is actively taken up by hyperactive thyroid cells. Once incorporated, I^{131} destroys the cells. This is a permanent treatment for hyperthyroidism and frequently results in the individual becoming hypothyroid and requiring lifelong TH replacement.
- Partial or total **thyroidectomy** may be a treatment choice.
- **Percutaneous ethanol injection** of the thyroid is used for patients with benign thyroid nodule and those with increased surgical risk like cardiac or pulmonary diseases.

Thyrototoxic crisis (thyroid storm) is a rare but dangerous worsening of the thyrotoxic state in which **death can occur within 48 hours** without treatment.

The condition may develop spontaneously, but it usually occurs in individuals who have undiagnosed or partially treated Graves disease and are subjected to excessive stress, such as infection, pulmonary or cardiovascular disorders.

The symptoms of thyroid crisis are caused by the increased action of thyroxine (T4) and triiodothyronine (T3) exceeding metabolic demands.

The systemic symptoms of thyrotoxic crisis include hyperthermia; tachycardia, especially atrial tachydysrhythmias; high-output heart failure; agitation or delirium; and nausea, vomiting, or diarrhea contributing to fluid volume depletion.

Treatment

Includes:

- 1- The use of drugs that block TH synthesis (i.e., propylthiouracil or methimazole).
- 2- The use of beta-blockers for control of cardiovascular symptoms.
- 3- Steroids or iodine (e.g., saturated solution of potassium iodide).
- 4- Supportive care.

**Thank
you**