# The Physiology of the Thyroid Gland

The **thyroid gland** is a butterfly-shaped endocrine organ located in the anterior neck, just inferior to the larynx, spanning the C5 to T1 vertebral levels. It consists of two lateral lobes connected by a thin bridge called the **isthmus**, which lies over the trachea.

## Structure and Histology

The thyroid is composed of multiple **spherical follicles**, the functional units of the gland. Each follicle is lined by **follicular cells (thyrocytes)** and filled with a protein-rich colloid containing **thyroglobulin**, a precursor to thyroid hormones. Scattered between follicles are **parafollicular cells (C cells)** that secrete **calcitonin**, a hormone involved in calcium homeostasis

## Hormones of the Thyroid Gland

The thyroid gland produces three main hormones:

1. **Thyroxine (T4)** – the primary hormone secreted, biologically less active
2. **Triiodothyronine (T3)** – the active form, mostly produced by peripheral conversion of T4
3. **Calcitonin** – a peptide hormone involved in calcium regulation, secreted by C cells

## Biosynthesis of Thyroid Hormones

The synthesis of T3 and T4 involves several tightly regulated steps

1. **Iodide uptake** – Follicular cells actively transport iodide from the blood via the sodium-iodide symporter.
2. **Iodide oxidation and organification** – Iodide is oxidized by thyroid peroxidase (TPO) and binds to tyrosine residues on thyroglobulin to form **monoiodotyrosine (MIT)** and **diiodotyrosine (DIT)**.
3. **Coupling reaction** – TPO mediates the coupling of MIT and DIT to form T3 (MIT + DIT) and T4 (DIT + DIT).
4. **Storage** – The iodinated thyroglobulin is stored in the colloid within follicles.
5. **Release** – Upon stimulation, colloid is endocytosed, and T3 and T4 are cleaved and released into the bloodstream.

## Regulation: Hypothalamic-Pituitary-Thyroid Axis

Thyroid function is regulated by the **hypothalamic-pituitary-thyroid (HPT) axis**

- The **hypothalamus** secretes **thyrotropin-releasing hormone (TRH)**.
- TRH stimulates the **anterior pituitary** to release **thyroid-stimulating hormone (TSH)**.
- TSH binds to receptors on thyroid follicular cells, stimulating hormone synthesis and release.

This axis operates via **negative feedback** . Elevated levels of circulating free T3 and T4 inhibit TRH and TSH production, while low hormone levels stimulate them.

## Actions of Thyroid Hormones

Thyroid hormones have **widespread systemic effects** , primarily by binding to nuclear receptors that regulate gene transcription

- **Basal Metabolic Rate (BMR)** – Increase oxygen consumption and heat production in most tissues.
- **Cardiovascular system** – Increase heart rate, cardiac output, and myocardial contractility.
- **Growth and development** – Essential for normal growth in children and fetal brain development.
- **Metabolism** – Enhance glucose absorption, lipid mobilization, and protein turnover.
- **Neuromuscular system** – Promote synaptic development and reflexes.

## Peripheral Conversion of T4 to T3

Only about **20 percent of T3** is secreted directly from the thyroid gland. The rest is formed peripherally by **deiodinases** :

- **Type I and II deiodinases** convert T4 to active T3.
- **Type III deiodinase** converts T4 to **reverse T3 (rT3)** , an inactive form.

This peripheral conversion allows fine-tuned control of thyroid hormone activity in different tissues

## Calcitonin and Calcium Homeostasis

Although not involved in metabolism, **calcitonin** helps regulate blood calcium by:

- Inhibiting osteoclastic bone resorption
- Promoting calcium deposition in bones
- Decreasing calcium reabsorption in the kidneys

Its role is relatively minor compared to **parathyroid hormone (PTH)** and **vitamin D**

## High-Yield Notes

- **Primary hormone secreted** : T4 (inactive), converted to T3 (active) in tissues.
- **TSH stimulates** : Iodide uptake, hormone synthesis, and thyroid growth.
- **Main hormone regulator** : Hypothalamus-pituitary-thyroid axis.
- **Function** : Controls metabolic rate, thermogenesis, cardiovascular output, and CNS development.
- **Disorders** : Graves disease (hyperthyroidism), Hashimoto’s thyroiditis (hypothyroidism), thyroid storm (life-threatening thyrotoxicosis).