

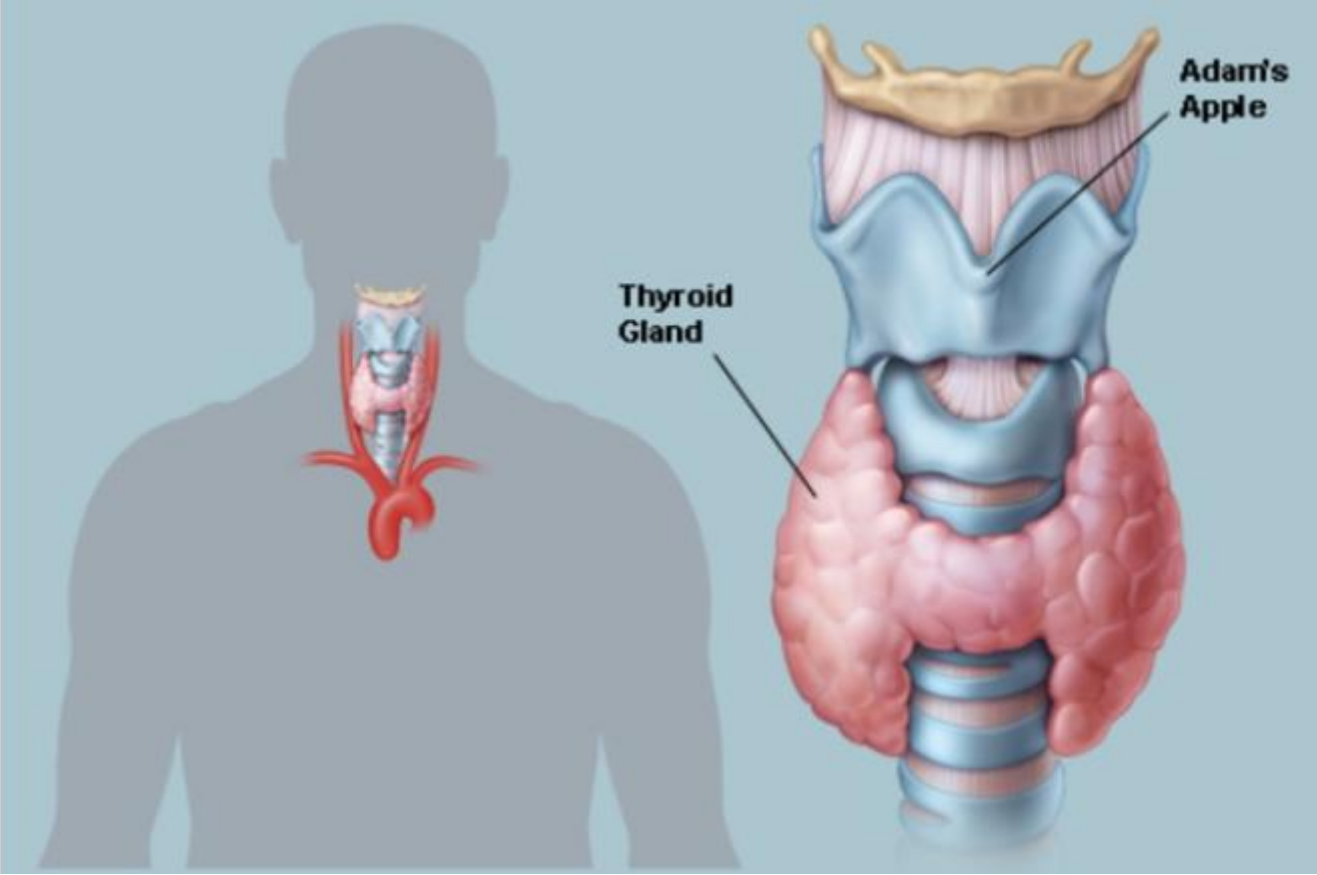
DEVELOPMENTAL BIOLOGY

TOPIC : THYROID GLAND

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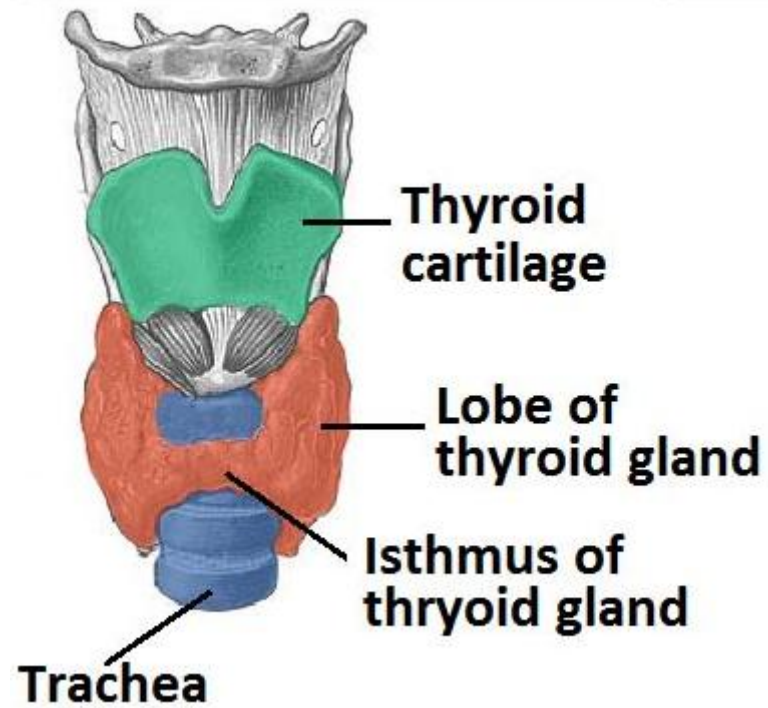
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THYROID GLAND



Anatomy

- The thyroid gland is a ductless **alveolar gland** found in the anterior neck, just below the laryngeal prominence (Adam's apple).
- It is roughly butterfly-shaped, with two lobes wrapping around the trachea and connected in the middle by an **isthmus**.



- It is supplied by superior and inferior **thyroid arteries**, drained via superior, middle and inferior **thyroid veins** and has a rich lymphatic system.

Cellular Structure

- The function of the Thyroid gland is to produce and store thyroid hormones.
- Thyroid epithelia form follicles filled with **colloid** – a protein-rich reservoir of the materials needed for thyroid hormone production.
- These follicles range in size from **0.02-0.3mm** and the epithelium may be simple cuboidal or simple columnar.

- In the spaces between the follicles, **parafollicular cells** can be found.
- These cells secrete calcitonin, which is involved in the regulation of calcium metabolism in the body.

Function

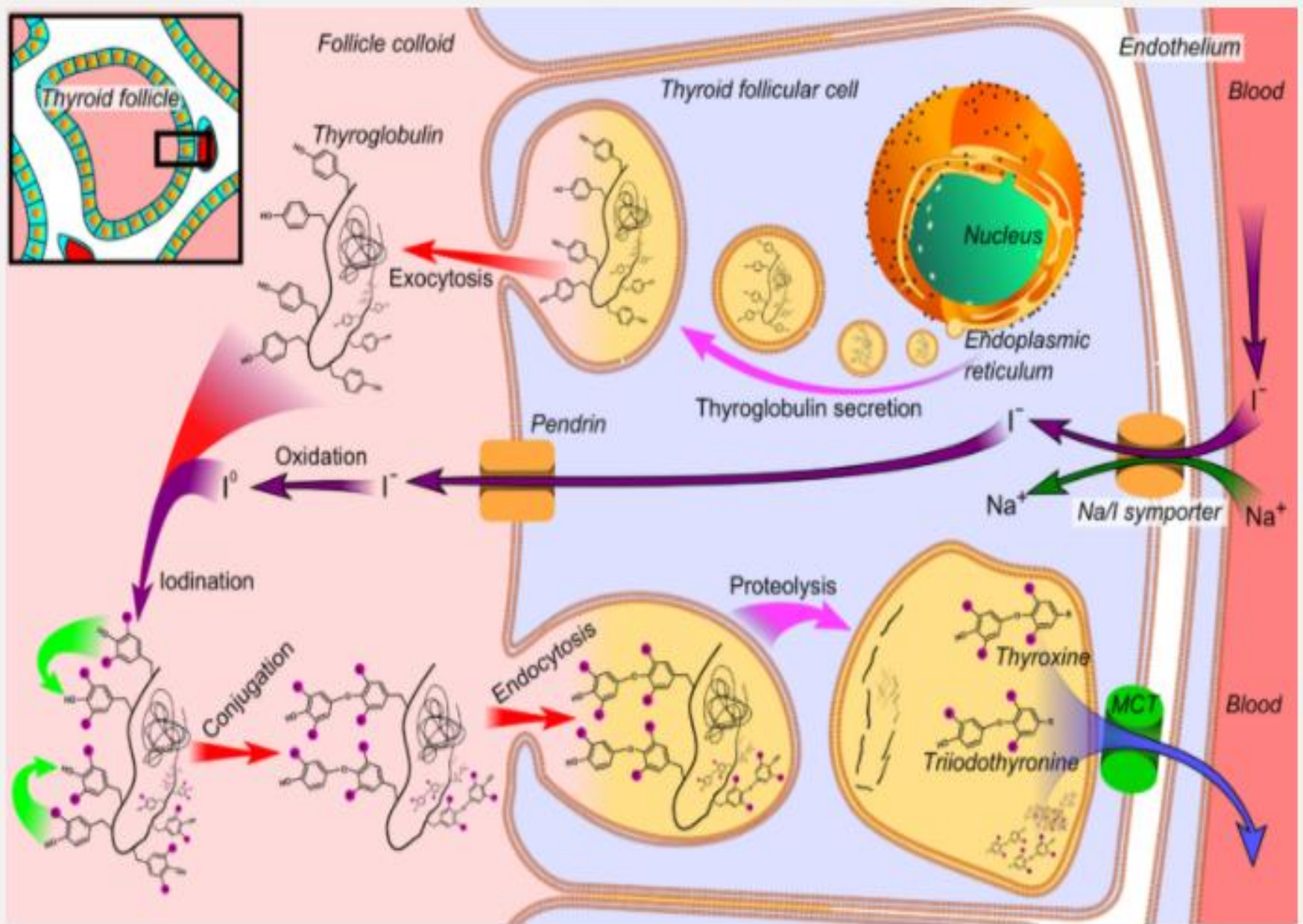
- The thyroid gland is one of the main regulators of **metabolism**.
- T3 and T4 typically act via **nuclear receptors** in target tissues and initiate a variety of metabolic pathways.
- High levels of them typically cause these processes to occur faster or more frequently.

- Metabolic processes increased by thyroid hormones include:
- Basal Metabolic Rate
- Gluconeogenesis
- Glycogenolysis
- Protein synthesis
- Lipogenesis
- Thermogenesis

- This is achieved in a number of ways, such as increasing the size and number of **mitochondria** within cells,
- increasing Na-K pump activity and
- increasing the presence of β -adrenergic receptors in tissues such as cardiac muscle.

Thyroid Hormone Synthesis

- There are six steps in the synthesis of thyroid hormone,
- **Active transport of iodide** into the follicular cell via the Sodium-Iodide Symporter (NIS). This is actually secondary active transport, and the sodium gradient driving it is maintained by a Sodium-Potassium ATPase.



- **Thyroglobulin (Tg)**, a large protein rich in Tyrosine, is formed in follicular ribosomes and placed into secretory vesicles.
- **Exocytosis** of Thyroglobulin into the follicle lumen, where it is stored as colloid. Thyroglobulin is the scaffold upon which thyroid hormone is synthesised.

- **Iodination** of the Thyroglobulin.
- Iodide is made reactive by the enzyme **thyroid peroxidase**.
- Iodide binds to the benzene ring on Tyrosine residues of Thyroglobulin, forming monoiodotyrosine (MIT) then diiodotyrosine (DIT).

- **Coupling** of MIT and DIT gives the Triiodothyronine (T3) hormone and coupling of DIT and DIT gives the Tetraiodothyronine (T4) hormone, also known as **Thyroxine**.

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- **Endocytosis** of iodinated thyroglobulin back into the follicular cell.
- Thyroglobulin undergoes proteolysis in lysosomes to cleave the iodinated tyrosine residues from the larger protein.
- Free T3 or T4 is then released, and the Thyroglobulin scaffold is recycled.

- T3 and T4 are the active thyroid hormones.
- They are **fat soluble** and mostly carried by plasma proteins – Thyronine Binding Globulin and Albumin.

- While T3 is the more potent form, it also has a shorter half-life due to its lower affinity for the binding proteins.
- Less than **1%** of T3 and T4 is unbound free hormone.

Thyroid Hormone Release

- Thyroid hormones are released as part of the hypothalamic-pituitary-thyroid axis.
- The Hypothalamus detects a low plasma concentration of thyroid hormone and releases **Thyrotropin-Releasing Hormone** (TRH) into the hypophyseal portal system.

- TRH binds to receptors found on thyrotrophic cells of the anterior pituitary gland, causing them to release **Thyroid Stimulating Hormone** (TSH) into the systemic circulation.

- TSH binds to TSH receptors on the basolateral membrane of thyroid follicular cells and induces the synthesis and release of thyroid hormone.

THYROID –PATHOPHYSIOLOGY.

- A **Goitre** is the medical term for an **enlarged thyroid gland**.
- The organ swells up to a palpable, and often visible, size within the neck.
- This may be due to an over or under active thyroid, iodine deficiency and in rare cases thyroid cancer.

- **Hyperthyroidism** is the medical term for an **overactive thyroid** gland.
- One common cause of Hyperthyroidism is **Grave's Disease** – an autoimmune condition where antibodies are produced that stimulate the TSH receptors on follicular cells.
- It affects roughly 1% of the population and is 10 times more common in women than in men.

- Patients may present with heat intolerance, weight loss, tachycardia, nervousness, increased sweating, exophthalmos and increased bowel movements.
- Hyperthyroidism can be treated with **Carbimazole** which inhibits iodine binding to thyroglobulin.

- **Hypothyroidism** is an **underactive thyroid** gland.
- One common cause of Hypothyroidism is **Hashimoto's Disease** – an autoimmune condition where thyroid follicles are destroyed or antibodies are produced that block the TSH receptor on follicle cells.

- Like hyperthyroidism, roughly 1% of the population is affected with it being 10 times more common in women than in men.
- In the developing world, the most common cause of Hypothyroidism is **iodine deficiency**.

- Patients can present with cold intolerance, weight gain, bradycardia, poor concentration, **myxoedema**, dry skin, some hair loss and constipation.
- Hypothyroidism can be treated with oral **T4** tablets (100-200 $\mu\text{g}/\text{day}$), to replace the hormone that is not being produced by the body.

Hyperthyroidism	Hypothyroidism
Anxiety	Depression
Restlessness	Fatigue
Tachycardia	Bradycardia
Weight loss	Weight gain
Thinning skin	Dry, itchy skin
Heat intolerance	Cold intolerance
Frequent bowel movements	Constipation
Goitre possible	Goitre possible
Low TSH	High TSH
High T3/T4	Low T3/T4

- **Thyroiditis**: Inflammation of the thyroid, usually from a viral infection or autoimmune condition.
- Thyroiditis can be painful, or have no symptoms at all.

- **Thyroid cancer:** An uncommon form of cancer, thyroid cancer is usually curable. Surgery, radiation, and hormone treatments may be used to treat thyroid cancer.

- **Thyroid nodule:** A small abnormal mass or lump in the thyroid gland. Thyroid nodules are extremely common. Few are cancerous. They may secrete excess hormones, causing hyperthyroidism, or cause no problems.

- **Thyroid storm:** A rare form of hyperthyroidism in which extremely high thyroid hormone levels cause severe illness.

Thyroid Hormones (Table 17.4)

Associated hormones	Chemical class	Effect
Thyroxine (T_4), triiodothyronine (T_3)	Amine	Stimulate basal metabolic rate
Calcitonin	Peptide	Reduces blood Ca^{2+} levels