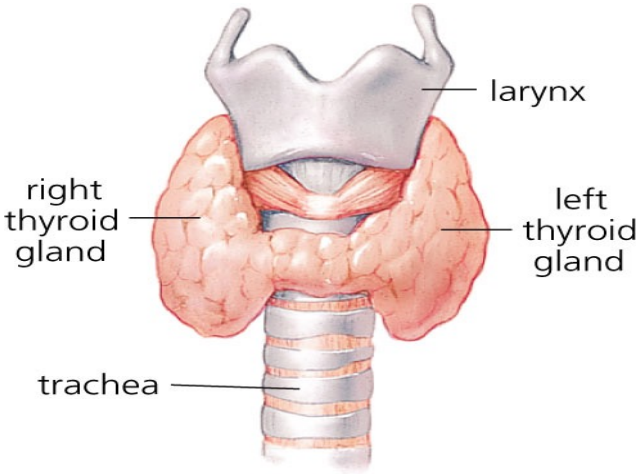
The Thyroid Gland

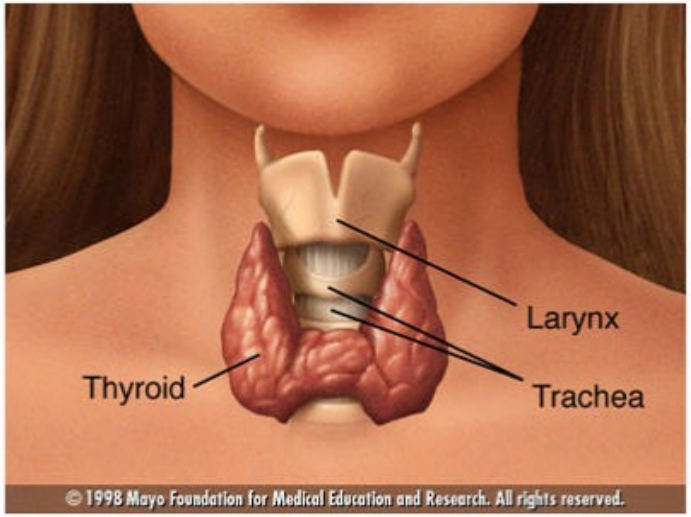
-Highly vascular flat structure.

-Located at the upper portion of the trachea.

- Composed of two lobes joined by an isthmus



- **Found in the neck;**



The thyroid gland is located at the base of your neck, just below your Adam's apple.

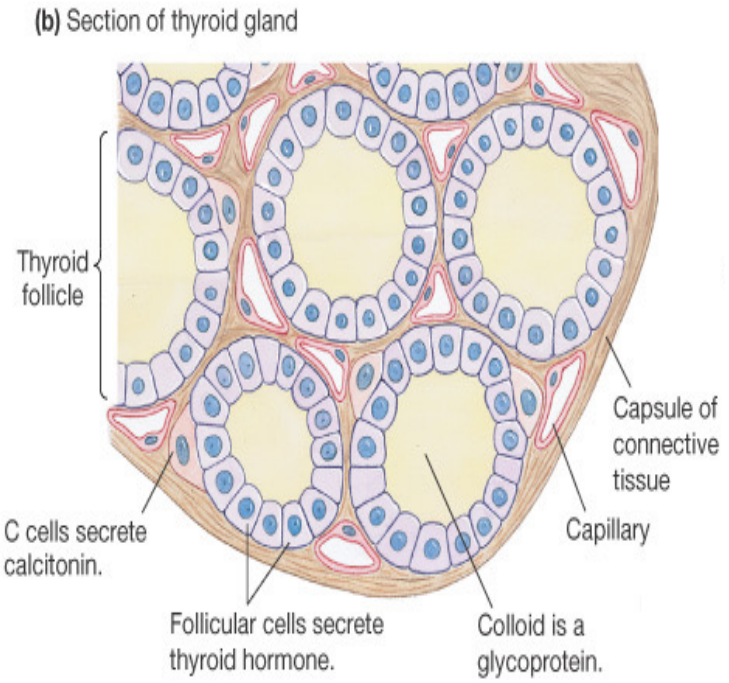
- responsible for the concentration of iodine & biosynthesis of thyroid hormones from Tyrosine
- Weighs 10-20g in adults
- Larger in women
- Plays a major role in the regulation of metabolism

Thyroid Gland: Hormones and Iodine Metabolism

Hormones of the Thyroid gland:

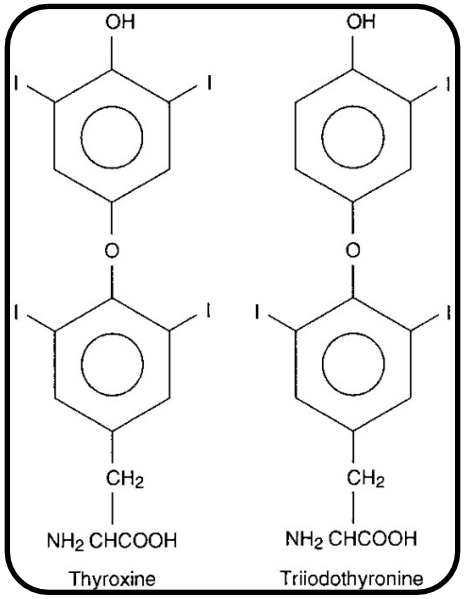
- **Parafollicular C-cells** secrets **calcitonin** (CT)
- **Follicule cells** secret;
  - – Amine hormones:
  - – **Thyroxine (tetraiodothyronine)**

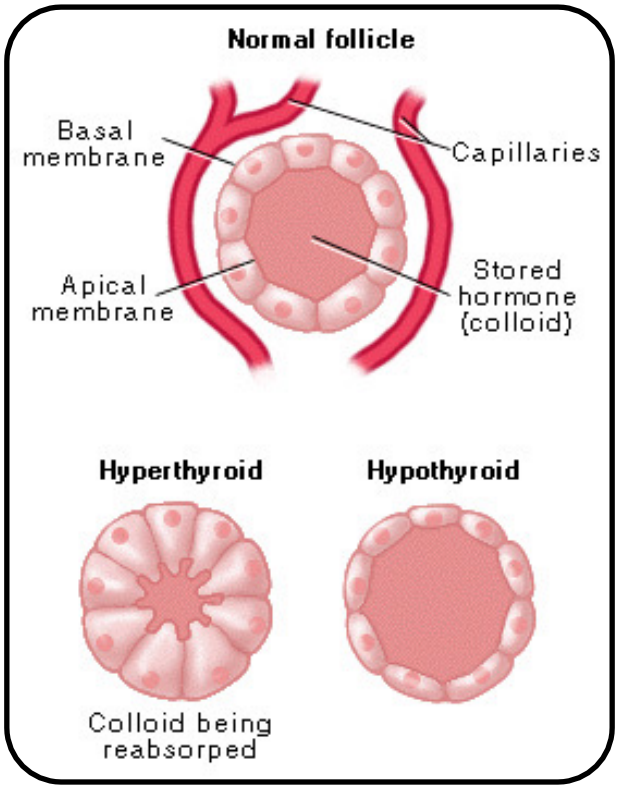
    T4 & triiodothyronine T_3
    - ↑ growth
    - ↑ metabolism
    - Thermogenic



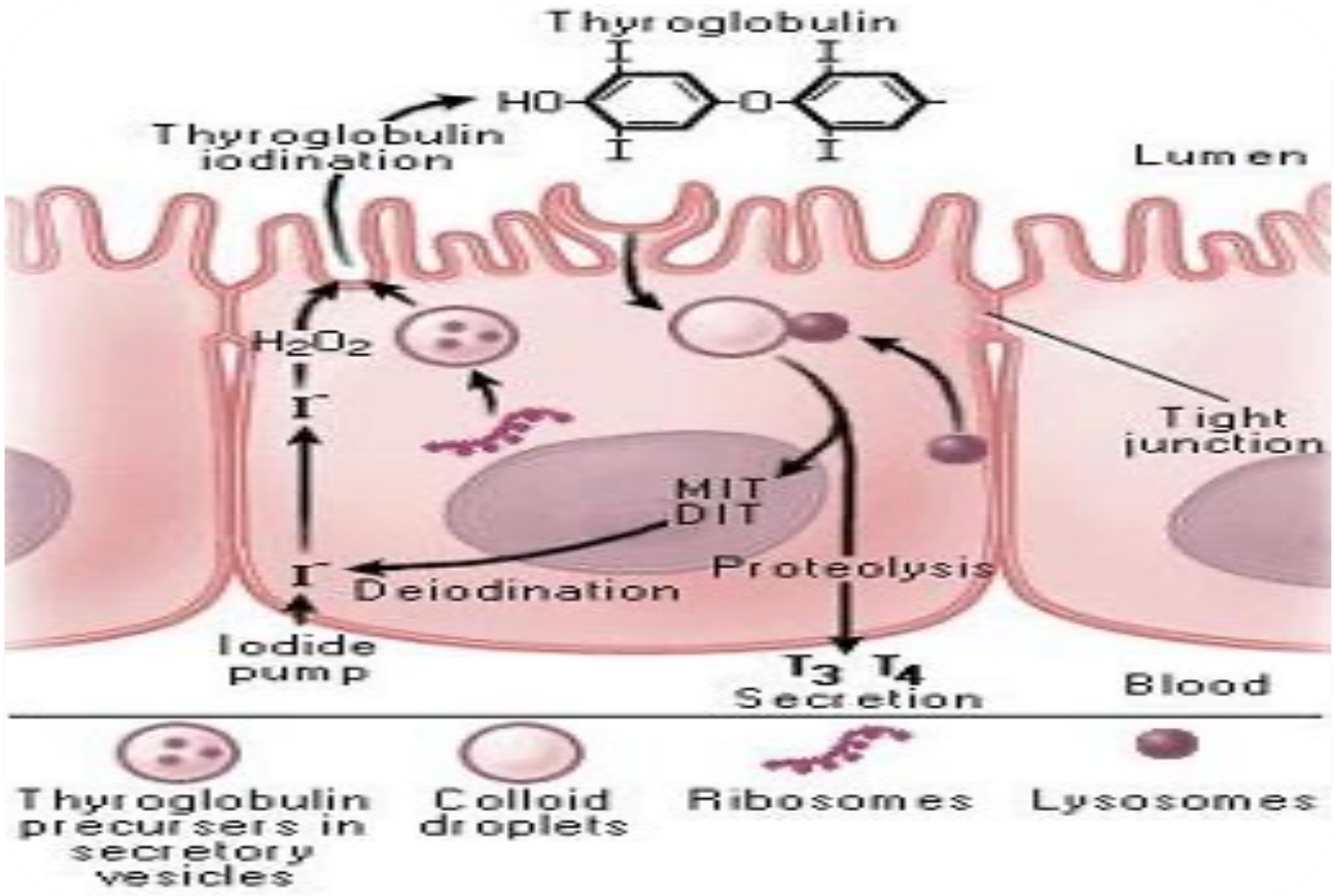
Thyroid Hormones

- Triiodothyronine (T_3) and Tetraiodothyronine (T_4)/Thyroxine
- Major secretory product is T_4
- 15% of T_3 is secreted by thyroid, the rest is produced in the peripheral tissues by the de-iodination of T_4
- Follicle consists of single layer of epithelial cells surrounding a sphere of colloid which contains the protein “Thyroglobulin”





- Recommended intake of iodine is 150µg/day to maintain hormone synthesis
- Dietary source of iodine is mainly fish
- Iodide should be added to foods (salt)



Thyroid Hormone:Transport

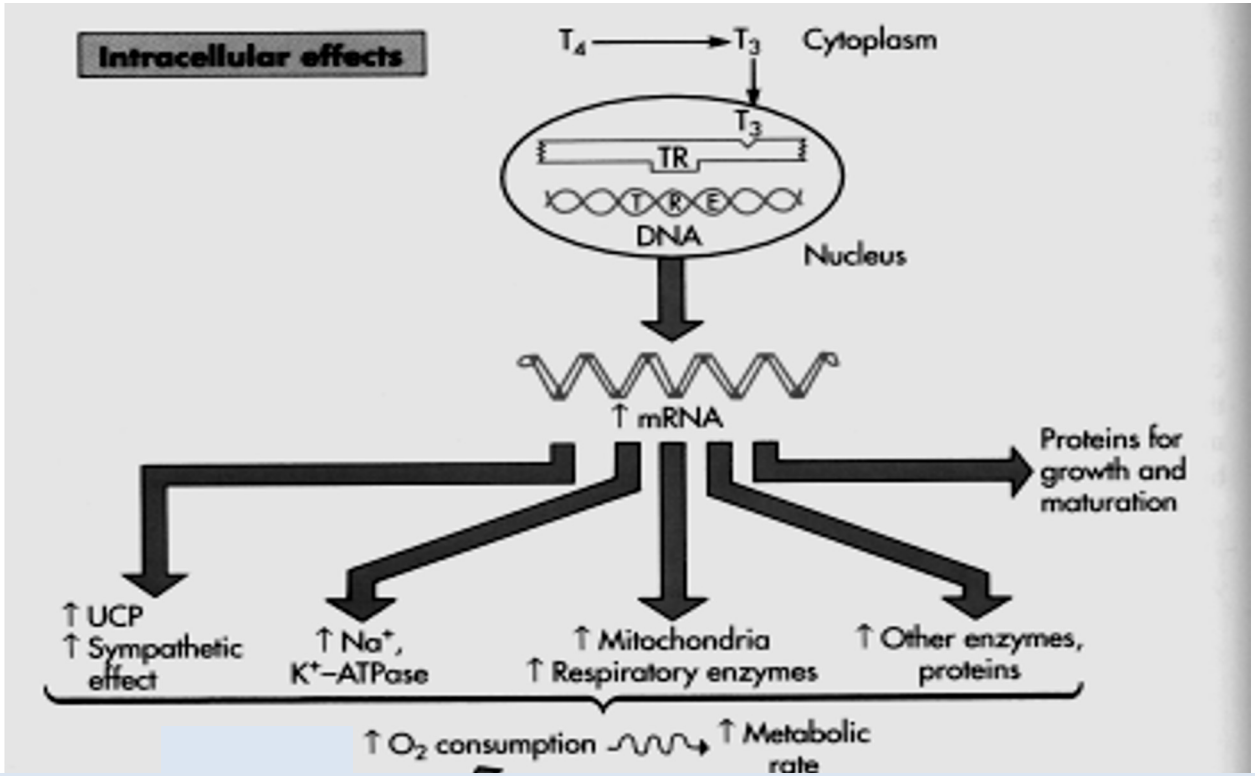
- T3 & T4 leave the thyroid gland by diffusion
- Both are transported in blood by three transport proteins, **Thyroxine binding globulin (TBG), transthyretin and albumin**
- A majority (70%) of T4 & T3 is bound to **TBG**
- Both enter their target cells by diffusion.
- Half life: 6- 7 days

Thyroxine and its precursors: Activity

- T4 mainly functions as a prohormone.

- T3 is the main active thyroid hormone and has the highest binding affinity for thyroid hormone receptor (TR).

Thyroxine and its precursors: Activity



TR: thyroid receptor.

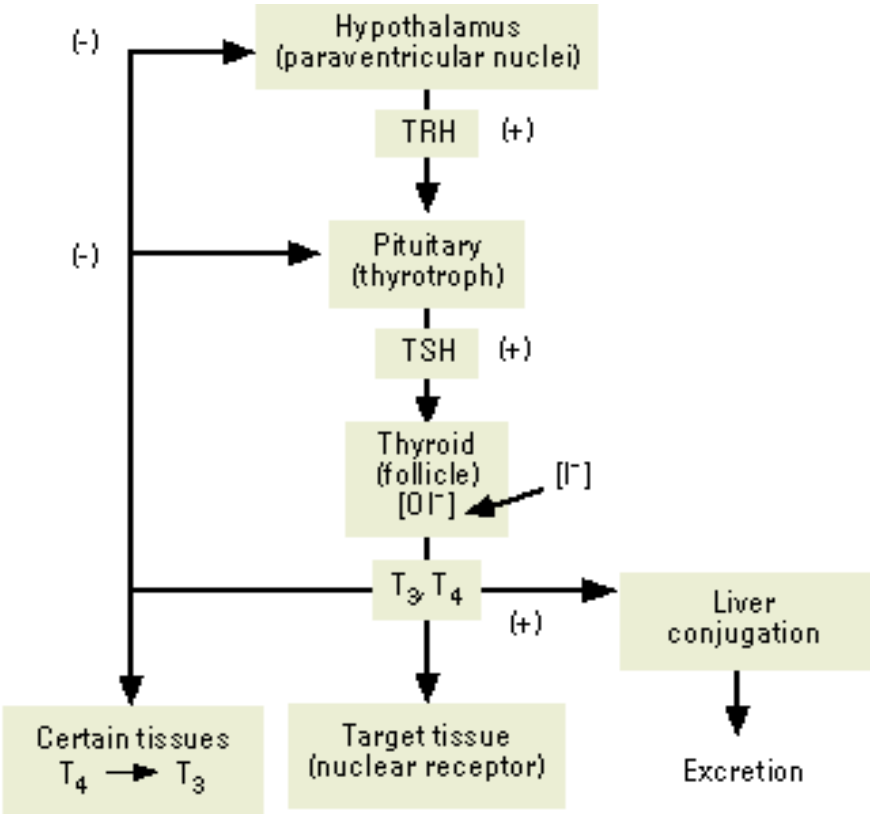
TRE: thyroid response element.

Actions of the Thyroid Hormones:

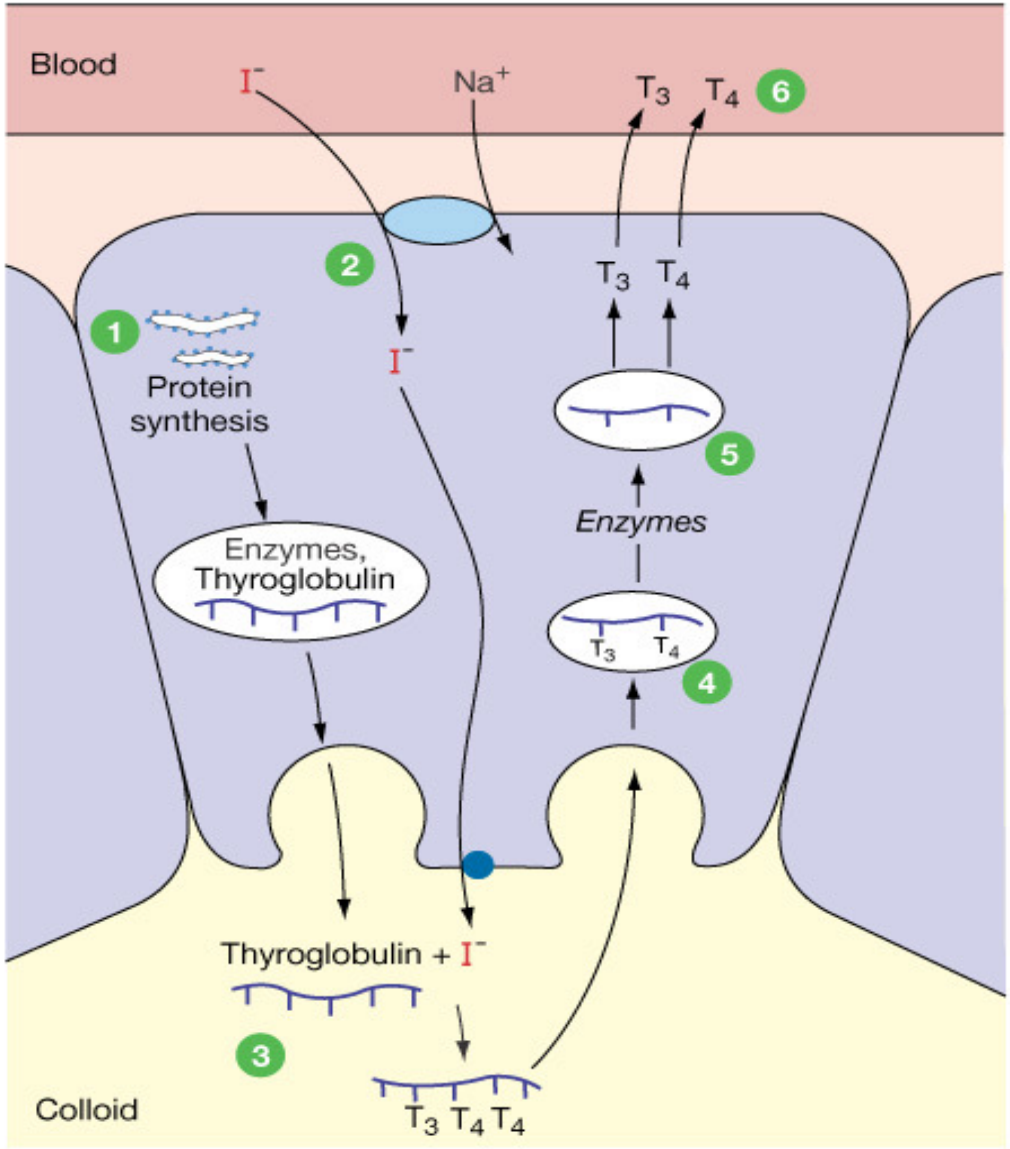
- Enhance growth and protein synthesis.
- Essential for the development of the nervous system.
- Increase oxygen consumption and basal metabolic rate.
- Increase body temperature “Calorigenic effect”.
- Cardiovascular effect:
    - Increase heart rate.
    - Increase force of contraction.

Regulation of thyroid Gland Activity

- Thyroid hormone feedback regulation of gland activity via suppression of TRH and TSH secretion.



Thyroxine and its precursors: Structure & Synthesis



1. Follicular cell synthesizes enzymes and thyroglobulin for colloid.
2. I^- is co-transported into the cell with Na^+ and transported into colloid.
3. Enzymes add iodine to thyroglobulin to make T_3 and T_4.
4. Thyroglobulin is taken back into the cell.
5. Intracellular enzymes separate T_3 and T_4 from the protein.
6. Free T_3 and T_4 enter the circulation.

Figure : Thyroid hormone synthesis

Biosynthesis

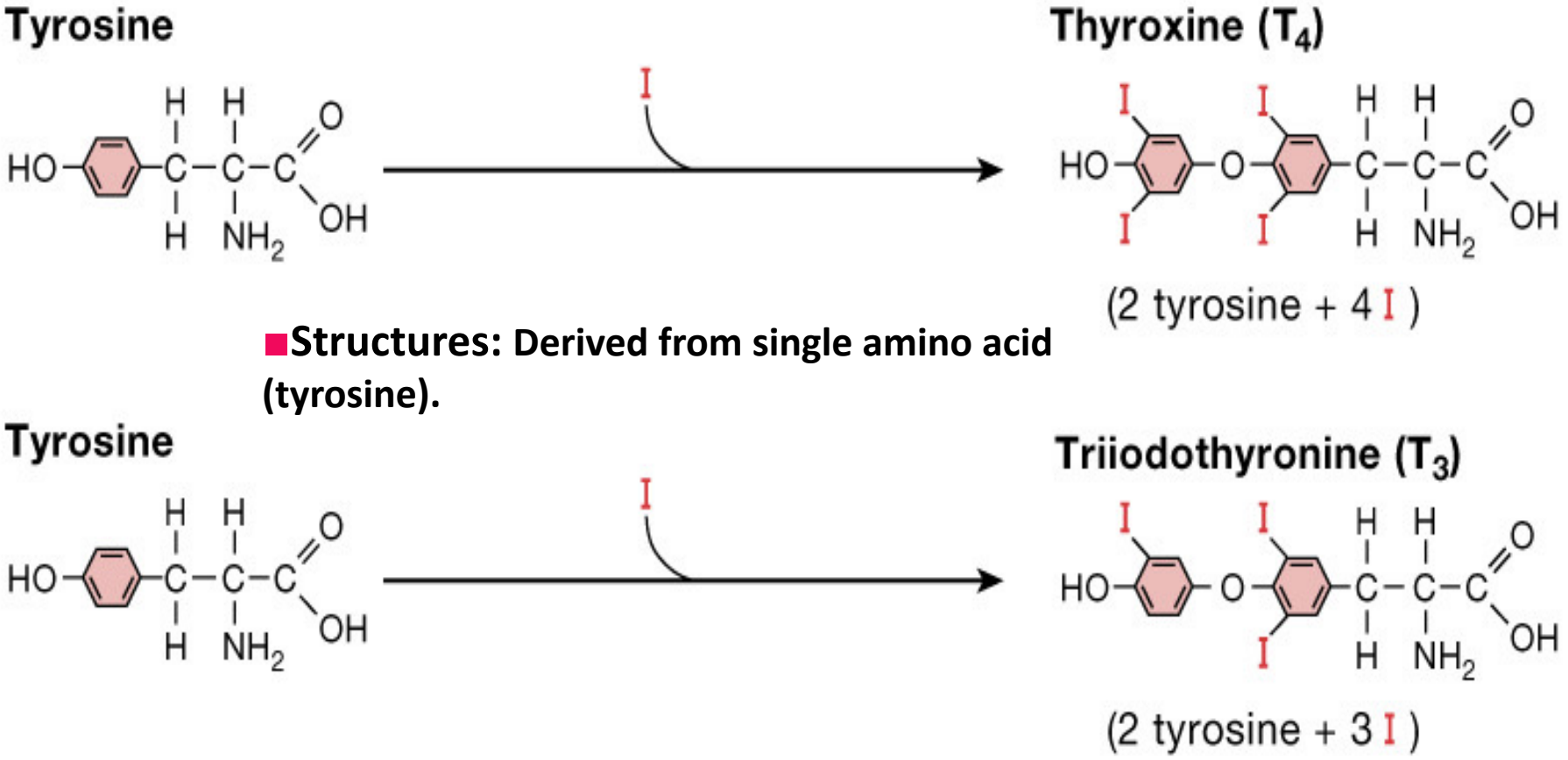
- Iodine **actively transported** to the thyroid gland under the influence of **TSH**. This is an energy-dependent process and is linked to **the Na+-K+ ATPase.**
- **Thyroid Peroxidase** Enzyme (**TPO**) convert Iodine to to a higher valence state, **iodide** (I+) using **hydrogen peroxide** as an oxidizing agent.
- **TPO** catalyze **coupling of Iodide with tyrosine residues of thyroglobulin to form monoiodotyrosine (MIT) and diiodotyrosine (DIT)**.
- The **coupling** of two DIT molecules to form T4—or of an MIT and DIT to form T3—occurs within the thyroglobulin molecule.

DIT + DIT → T4

DIT + MIT → T3

- Thyroxine **stored as Thyroglobulin.**
- **TSH** enhances lysosomes to release Thyroxine from Thyroglobulin.
- **5′-Deiodinase** convert Thyroxine (T4) to Triiodothyronine (T3) mainly in the peripheral tissues (80%).

Thyroxine and its precursors: Structure & Synthesis



- **Structures: Derived from single amino acid (tyrosine).**

Figure : Thyroid hormones are made from tyrosine and iodine

- The thyroid hormones T3 and T4 are unique in that **iodine** (as iodide) is an **essential** component of both and require iodine for their **bioactivity.**
- These hormones; they are synthesized as part of thyroglobulin; they are **stored** in an intracellular reservoir (**colloid**)

- **Thyroglobulin is the precursor of T4 and T3.**

- It contains **115 tyrosine residues**, each of which is a potential site of iodination.

- About **70%** of the iodide in thyroglobulin exists in the inactive precursors,**monoiodotyrosine (MIT) and diiodotyrosine (DIT),** while **30% is in the iodothyronyl residues, T4 and T3.**

Structure Activity Relation Ship:

- Angle between the two aromatic rings must be 120^0.

- Triiodothyronine is 4 times more active than Thyroxine.

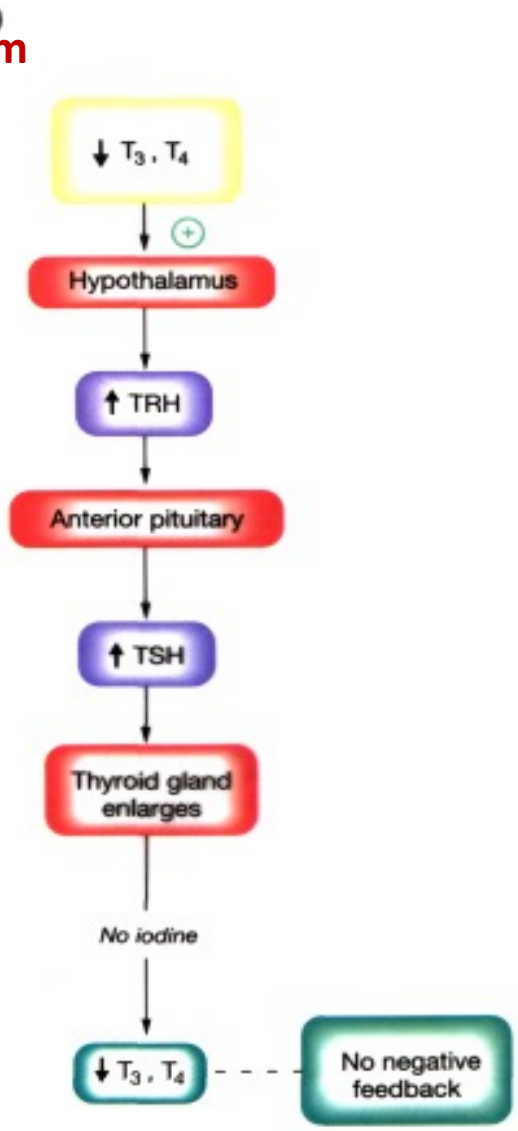
Disease Due to Hypothyroidism:

- **Hypothyroidism** – lack of thyroid hormone in tissues; can **be primary** (failure of thyroid), **secondary** (failure of pituitary) or **tertiary** (disorder of hypothalamus)
- **Goiter**: – enlargement of the gland because of increased stimulation of TSH
    - Causes: Lack of iodine in diet.
    - Symptoms:
        - » Enlargement in the thyroid gland (Thyroid Hypertrophy).
        - » Low level of thyroxine.
        - » High level of TSH.
    - Treatment: Iodine.

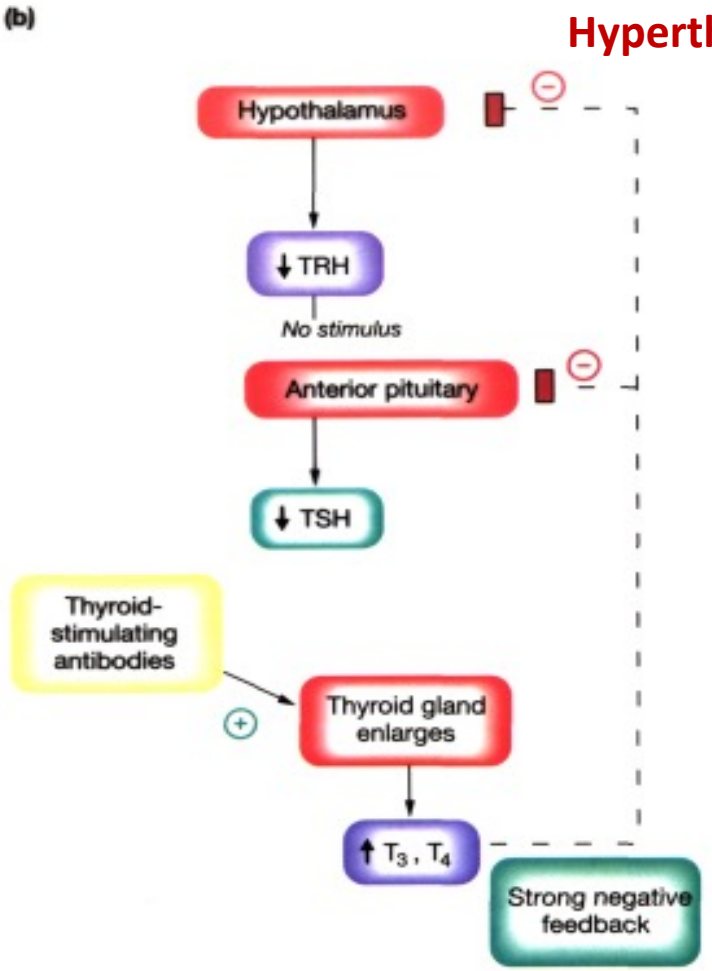
- **Cretinism**:
    - Irreversible condition due to deficiency of thyroxine soon after birth.
    - Retardation in Physical and Mental development.

T3 & T4 Control Pathways & Diseases from Malfunction

a-Goiter
Hypothyrodism



b-Graves' disease
Hyperthyrodism



- **Myxedema**:
  - Deficiency **of thyroxine in adults** due to:
    - » Removal of thyroid gland by surgery.
    - » Destruction of the gland by Radioactive Iodine.
    - » Atrophy of the thyroid gland.
  - Symptoms:
    - » Muscle weakness.
    - » Poor appetite.
    - » Slow heart rate
    - » Dry cold skin
  - Treatment:
    - » Thyroxine for life.

Disease Due to Hyperthyroidism:

- **Thyrotoxicosis:**

  excess action of the thyroid hormones (hyperactivity, nervousness, **fatigue, palpitations, sweating…)**

- **Graves' disease (Diffuse Toxic Goiter):**
  - Causes: Autoimmune disease resulted in Enlargement and excessive secretion of the thyroid gland and the most common cause of hyperthyroidism (**increaseT3 & T4 hormones levels , decrease TSH and TRH)**
  - Symptoms:
    - » Enlargement in the thyroid gland (Thyroid Hypertrophy).
    - » Protrusion of the eye balls.
    - » High body temperature and flushes.

- Thyroid cancer:
- Treatment: Antithyroid drugs.