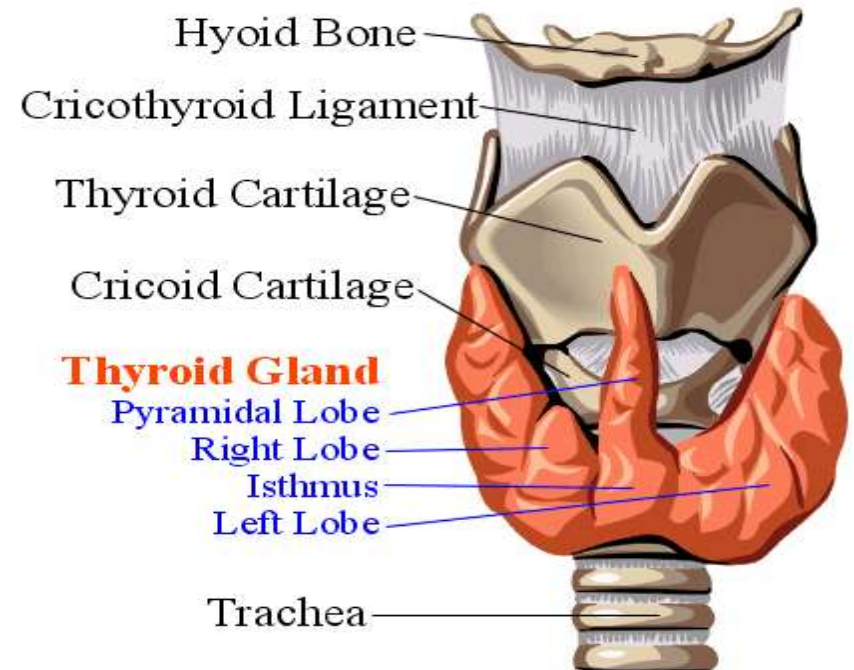
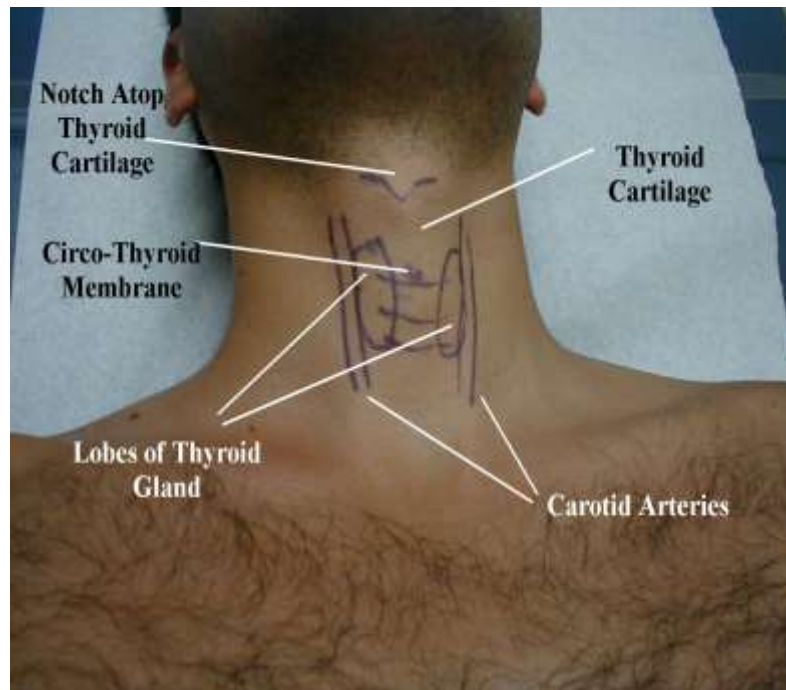


Thyroid Hormones

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The Thyroid Gland

- Normal gland weighs about 20g
- Derived from embryonic endoderm.
- Consists of 2 lobes joined by a thin isthmus



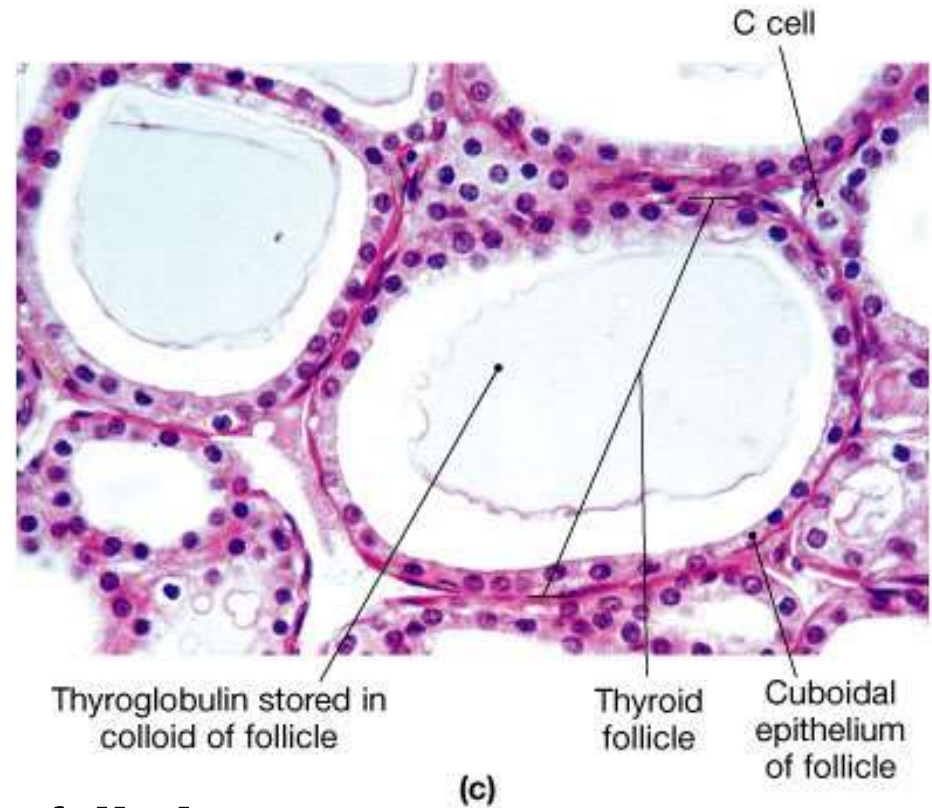
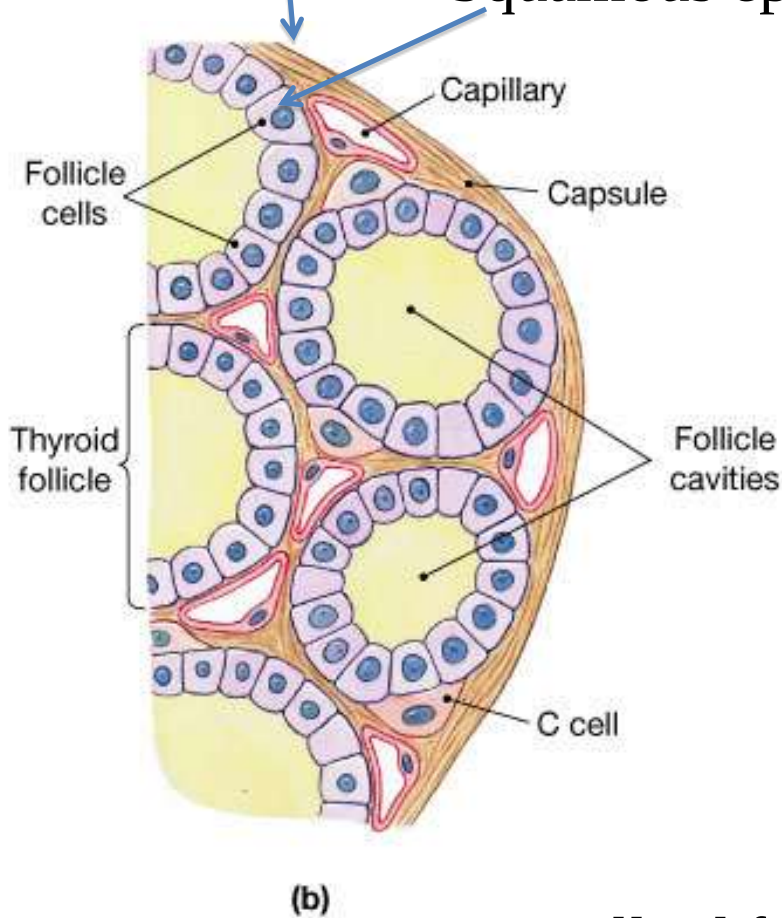
Histology of the Thyroid tissue

- The thyroid gland composed of closely packed sacs called **follicles**, composed of epithelial follicular cells and colloid.
 - Follicular cells: secrete thyroxine (T_4) and triiodothyronine (T_3).
 - Colloid, a jellylike substance inside a follicle that contain thyroglobulin.
- **Parafollicular cells** located outside the follicles, which secrete **calcitonin**.
- The thyroid gland is capable of storing **many weeks worth of thyroid hormone** (coupled to thyroglobulin).

The Thyroid Gland – Histology

Gland is composed of hollow spheres, called **colloid follicles**.

Squamous epithelial cells, cuboidal cells (follicle cells)



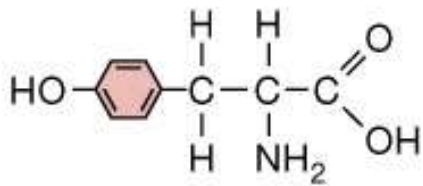
Colloid fills the follicle cavities

Follicle cells produce thyroglobulin $\xrightarrow{I}$ TH

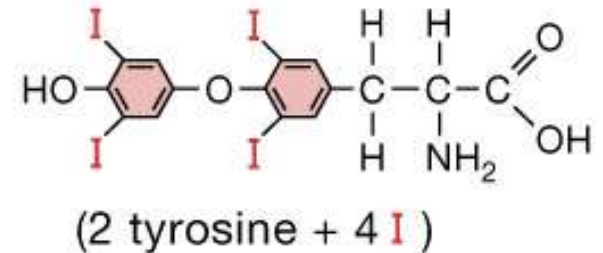
Thyroid Hormones - Structure

- There are two biologically active thyroid hormones:
 - **tetraiodothyronine** (T_4 ; usually called thyroxine)
 - triiodothyronine (T_3)
- Derived from modification of **tyrosine**.

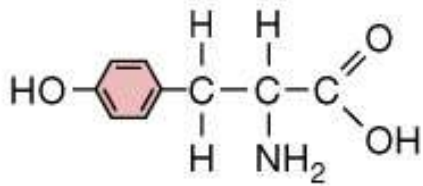
Tyrosine



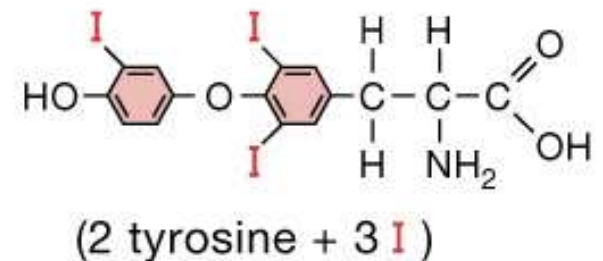
Thyroxine (T_4)



Tyrosine



Triiodothyronine (T_3)

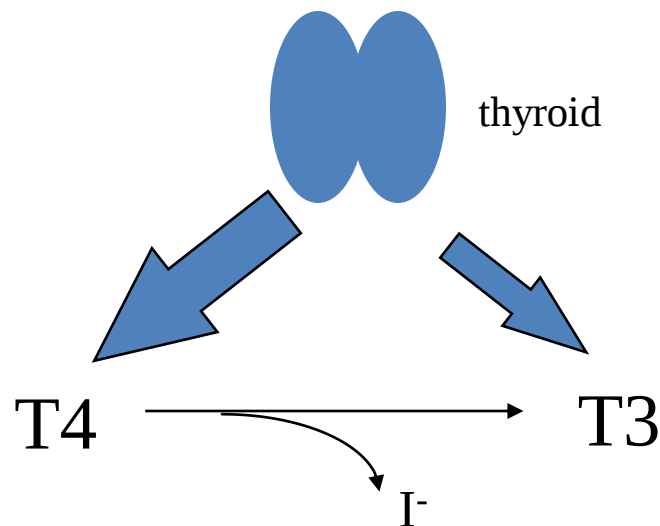


Thyroglobulin – Storage function

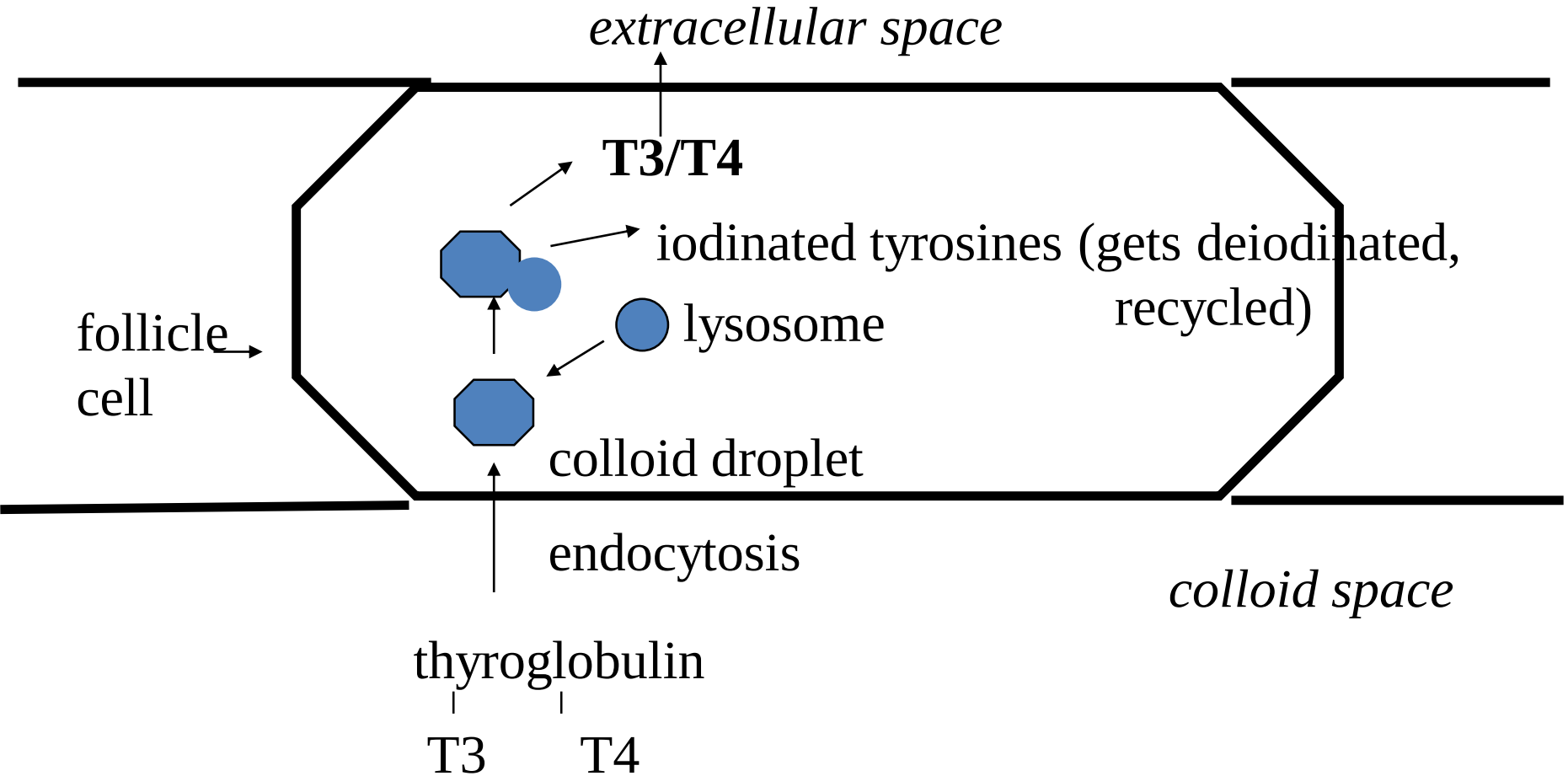
- Thyroglobulin is a very large Glycoprotein (10% carbohydrate).
- M. Wt. 660,000
- 2 identical subunits of 330,000 MW.
- 132 tyrosines and 25 to 30 iodinated.
- Thyroid hormones are attached to thyroglobulin and stored extracellularly in the follicle.
- The hormones are released after thyroglobulin is endocytosed and hydrolysed.
- Hydrolysis accomplished by lysosomal proteases inside the follicular cells.

Secretion of T_4 and T_3

- The thyroid secretes about 80 μg of T_4 , but only 5 μg of T_3 per day.
- However, T_3 has a much greater biological activity (about 10 times) than T_4 .
- An additional 25 $\mu\text{g}/\text{day}$ of T_3 is produced by **peripheral monodeiodination** of T_4 .



Utilization of Thyroglobulin to Secrete Thyroid Hormones



The role of Iodine in Thyroid Hormone Production

- Thyroid hormones are unique biological molecules in that they incorporate iodine in their structure.
- Thus, adequate iodine intake (diet, water) is required for normal thyroid hormone production.
- Major sources of iodine:
 - iodized salt
 - iodated bread
 - dairy products
 - shellfish
- Minimum requirement: 75 $\mu\text{g}/\text{day}$ which is about 10g of iodized salt.

Transport of Thyroid Hormones:

T_3 and T_4 (Iodothyronines)

- All are amino acid derivatives (tyrosine), not very soluble in water but are **lipid-soluble** (hydrophobic molecules).
- Thus, they are found in the circulation associated with binding proteins:
 - **Specific protein carrier called Thyroid hormone-binding globulin (TBG)**
 - 70% of T_3 and T_4
 - **Pre-albumin (Transthyretin)**
 - 10% of T_4 and very little of T_3
 - **Albumin**
 - 25% of T_3 and 15% of T_4
- Less than 1% of thyroid hormone is found free in the circulation.
- Only free and albumin-bound thyroid hormone is biologically available to tissues.

Regulation of Thyroid Hormone Levels

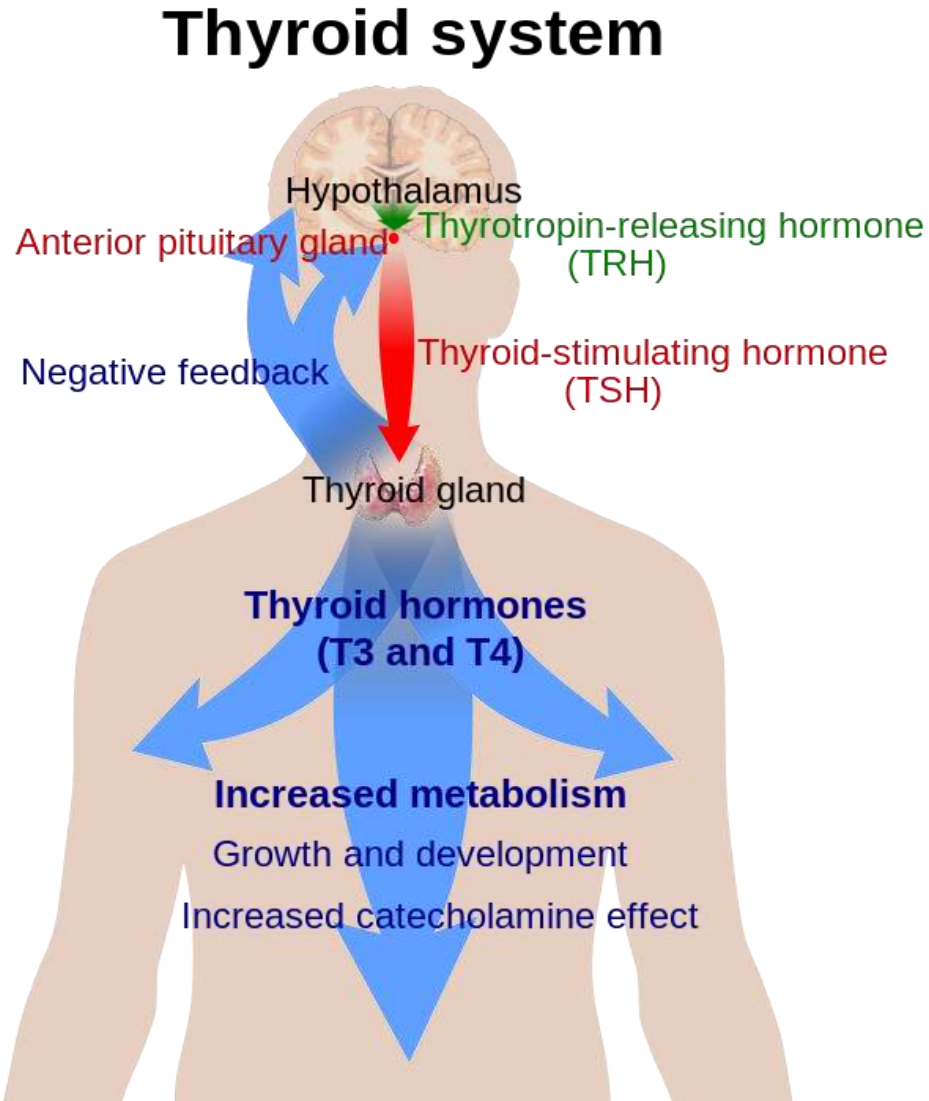
- Thyroid hormone synthesis and secretion is regulated by two main mechanisms:
 - an “autoregulation” mechanism, which reflects the available levels of iodine.
 - regulation by the hypothalamus and anterior pituitary

Autoregulation of Thyroid Hormone Production

- The rate of iodine uptake and incorporation into thyroglobulin is influenced by the amount of iodide available:
 - low iodide levels **increase iodine transport** into follicular cells
 - high iodide levels **decrease iodine transport** into follicular cells
- Thus, there is **negative feedback regulation** of iodide transport by iodide.

Regulation of TSH Release from the Anterior Pituitary

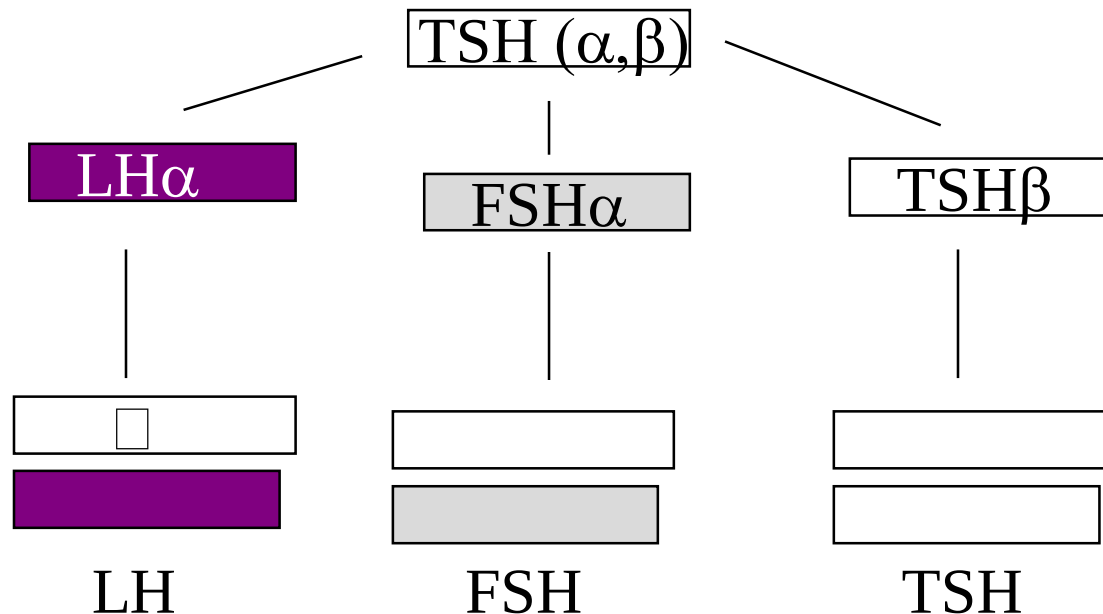
- TSH release is influenced by hypothalamic **TRH**, and by thyroid hormones themselves.
- Thyroid hormones exert negative feedback on TSH release at the level of the anterior pituitary.
 - inhibition of **TSH synthesis**
 - decrease in **pituitary receptors for TRH**



Neuroendocrine Regulation of Thyroid

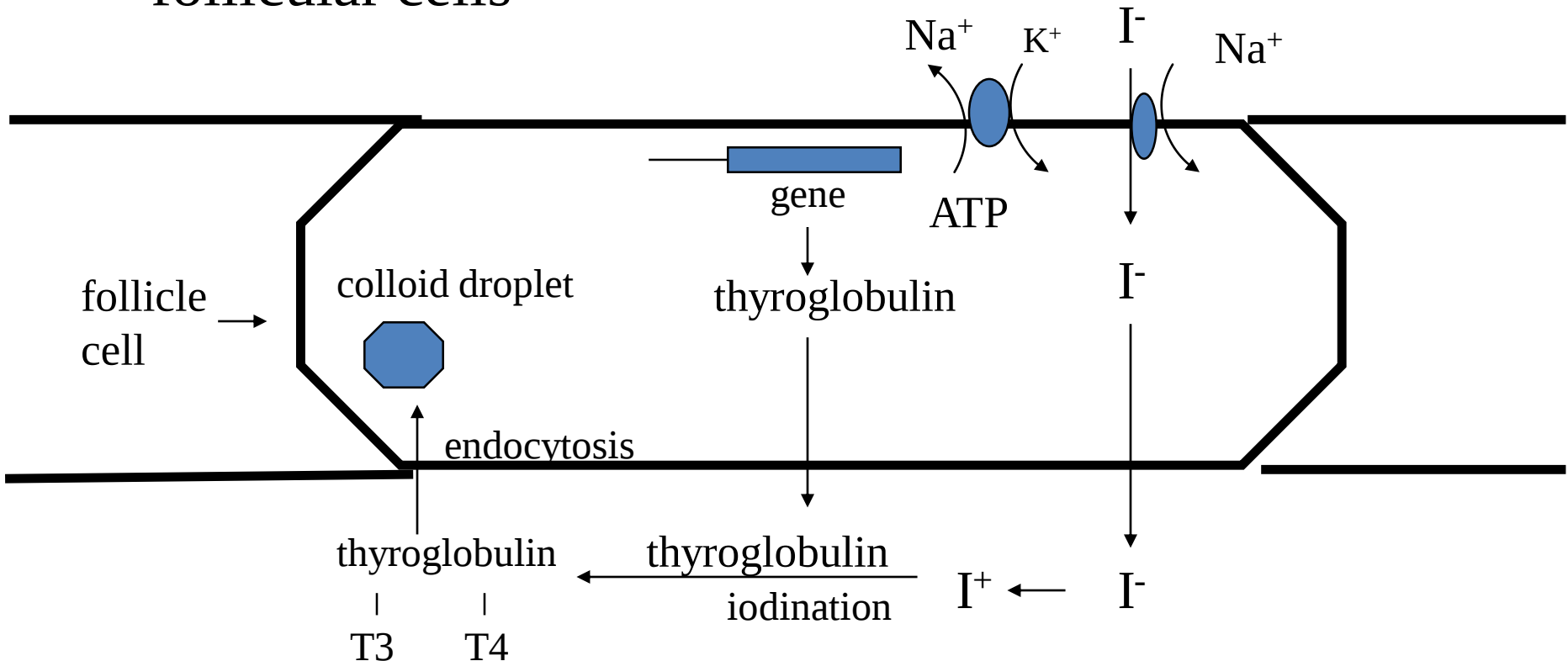
Hormones: Role of TSH

- Thyroid-stimulating hormone (TSH, also known as **thyrotropin**) is produced by **thyrotroph cells** of the anterior pituitary which regulates the endocrine function of the thyroid gland.
- TSH is a glycoprotein hormone composed of two subunits (**alpha and beta**):
 - TSH α subunit (common to hCG, LH, FSH)
 - TSH β subunit is unique to TSH, which gives specificity of receptor binding and biological activity



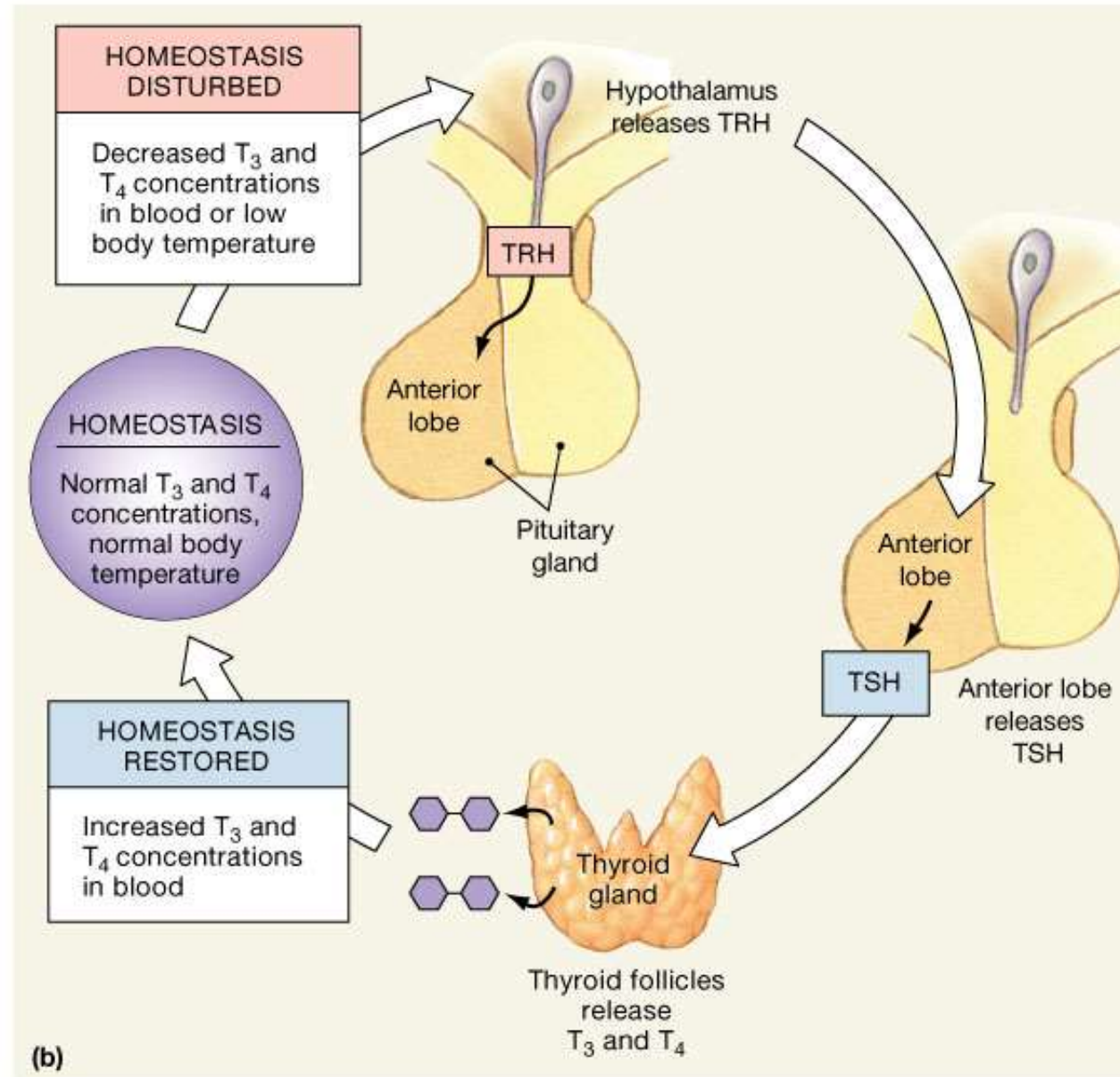
Action of TSH on the Thyroid

- TSH acts on follicular cells of the thyroid.
 - increases **iodide transport** into follicular cells
 - increases production and iodination of **thyroglobulin**
 - increases **endocytosis of colloid** from lumen into follicular cells



Regulation of T_4 and T_3 Secretion

All aspects of hormone synthesis are regulated by extra thyroid mechanism (TRH-TSH).



Actions of Thyroid Hormones

- Thyroid hormone stimulates **basal metabolic rate**.
- Maintain metabolic homeostasis by regulating:
 - Intermediary metabolism
 - Body weight
 - Oxygen requirements
 - Body temperature
- Thyroid hormones are essential for **normal growth of tissues**, including the nervous system.
- Also, positive controller of growth, reproduction and differentiation.
- Lack of thyroid hormone during development results in short stature and mental deficits (**cretinism**).

Effects of THs in Growth and Tissue Development

- THs are essential for linear growth & pubertal development
- Increase growth and maturation of bone
- Increase tooth development and eruption
- Mobilizes calcium from bone
- Increase growth and maturation of epidermis, hair follicles and nails
- Increase rate and force of skeletal muscle contraction
- Inhibits synthesis and increases degradation of mucopolysaccharides in subcutaneous tissue

Effects on the Nervous System

- Critical for normal CNS neuronal development
- Enhances wakefulness and alertness
- Enhances memory and learning capacity
- Required for normal emotional tone
- Increase speed and amplitude of peripheral nerve reflexes.

Effects on the Reproductive System

- Required for normal follicular development and ovulation in the female
- Required for the normal maintenance of pregnancy
- Required for normal spermatogenesis in the male

Dysfunction of Thyroid Gland

1. **Decreased thyroid hormone levels** - Hypothyroidism.
short stature (acquired), developmental delay (congenital).

- Low T4
- Possibly Low T3 too.
- Raised TSH (unless pituitary problem!)

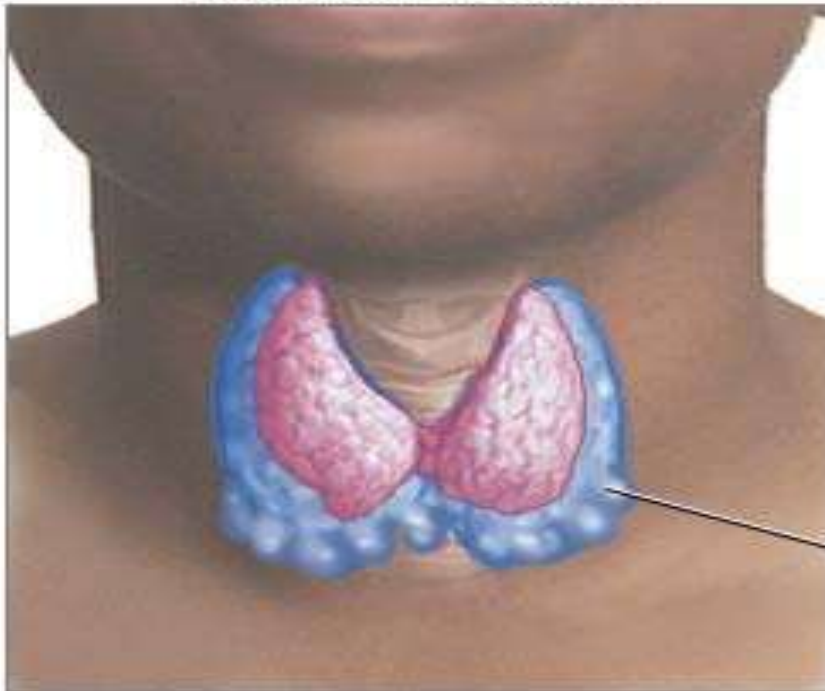
2. **Increased thyroid hormone levels** - Hyperthyroidism

Agitation, irritability, & weight loss.

- High T4 +/- High T3
- Low (suppressed) TSH

Autoimmune hypothyroidism

Hashimoto's disease



Enlarged, inflamed
hypofunctioning
thyroid (goiter)

Hashimoto's Disease

- Most common cause of hypothyroidism
- Autoimmune lymphocytic thyroiditis.
- Antithyroid antibodies:
 - Thyroglobulin Ab
 - Microsomal Ab
 - TSH-R Ab (block)
- Females > Males
- Runs in Families.

Clinical features of Acquired hypothyroidism

- Weight gain
- Goitre
- Short stature
- Fatigue
- Constipation
- Dry skin
- Cold Intolerance
- Hoarseness
- Sinus Bradycardia

Diagnosis:

- High TSH, low T4
- Thyroid antibodies

Treatment:

- Replacement thyroid hormone medication:
Thyroxin

Hyperthyroidism

Diagnosis:

- High TSH, free T3&T4.
- Thyroid antibodies (TSH receptors antibodies).
- Radionucleotide thyroid scan (increase uptake).
- **Isotope scan is very important**

Treatment:

- Radioactive iodine, anti-thyroid drugs & surgery.
- **Drugs:** *Beta*-blockers, Carbimazole and PTU (propylthiouracil)

Goiter



- A swollen thyroid gland

Causes:

- Congenital (maternal antithyroid drugs, maternal hyperthyroidism, dysmorphogenesis)
- Physiological (puberty)
- Iodine deficiency
- Graves disease
- Hashimoto thyroiditis
- Tumor