

THE THYROID GLAND

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OBJECTIVES

- LIST THYROID GLAND HORMONES
- DESCRIBE THE SYNTHESIS OF THE THYROID HORMONES
- DESCRIBE THE RELEASE AND ACTIONS OF THYROID HORMONES
- DESCRIBE THE NEGATIVE FEEDBACK MECHANISMS (CONTROL)

- **It is located below the larynx on either sides and anterior to the trachea.**
- **The first recognized endocrine gland.**

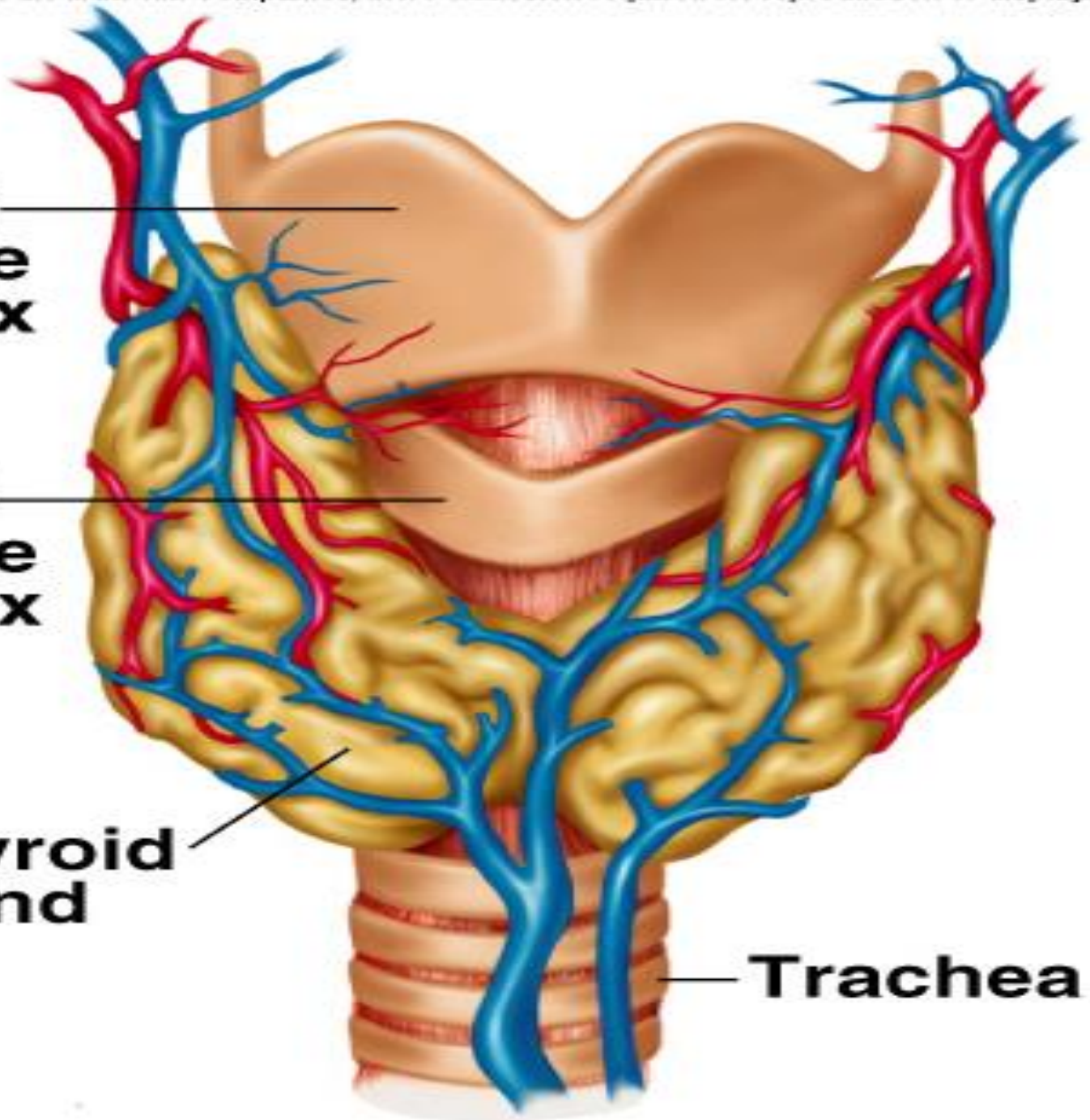
**Thyroid
cartilage
of larynx**

**Cricoid
cartilage
of larynx**

**Thyroid
gland**

Trachea

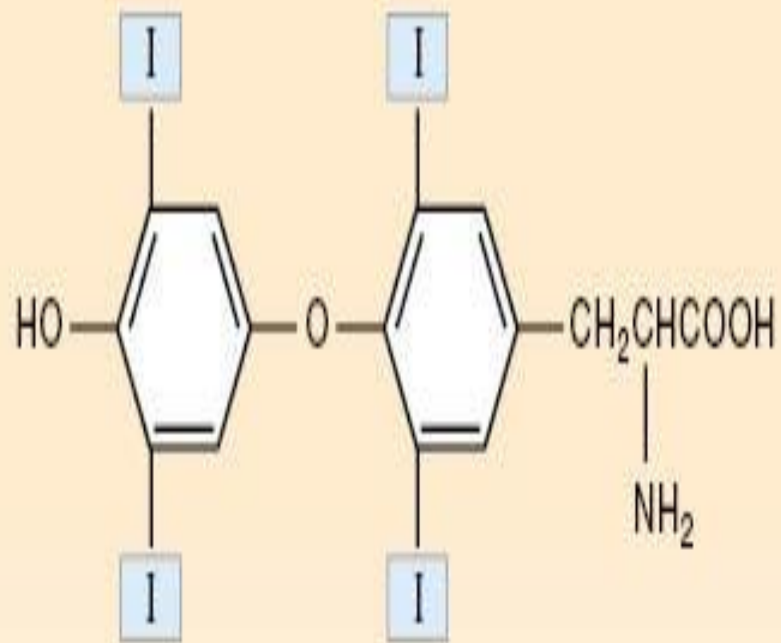
(a)



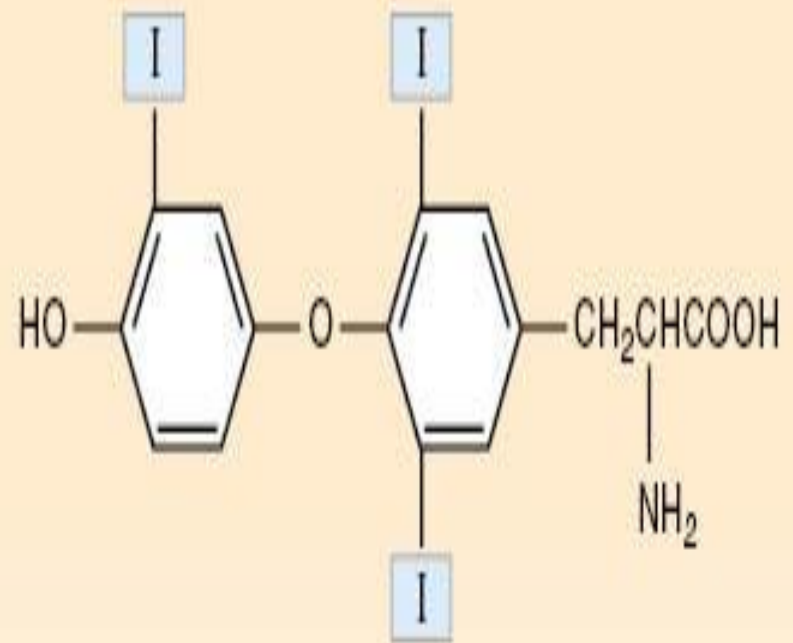
HORMONES

- T3 Triiodothyronine **10%.**
- T4 thyroxine (tetraiodothyronine) **90%.**
- Reverse T3
- Calcitonin.

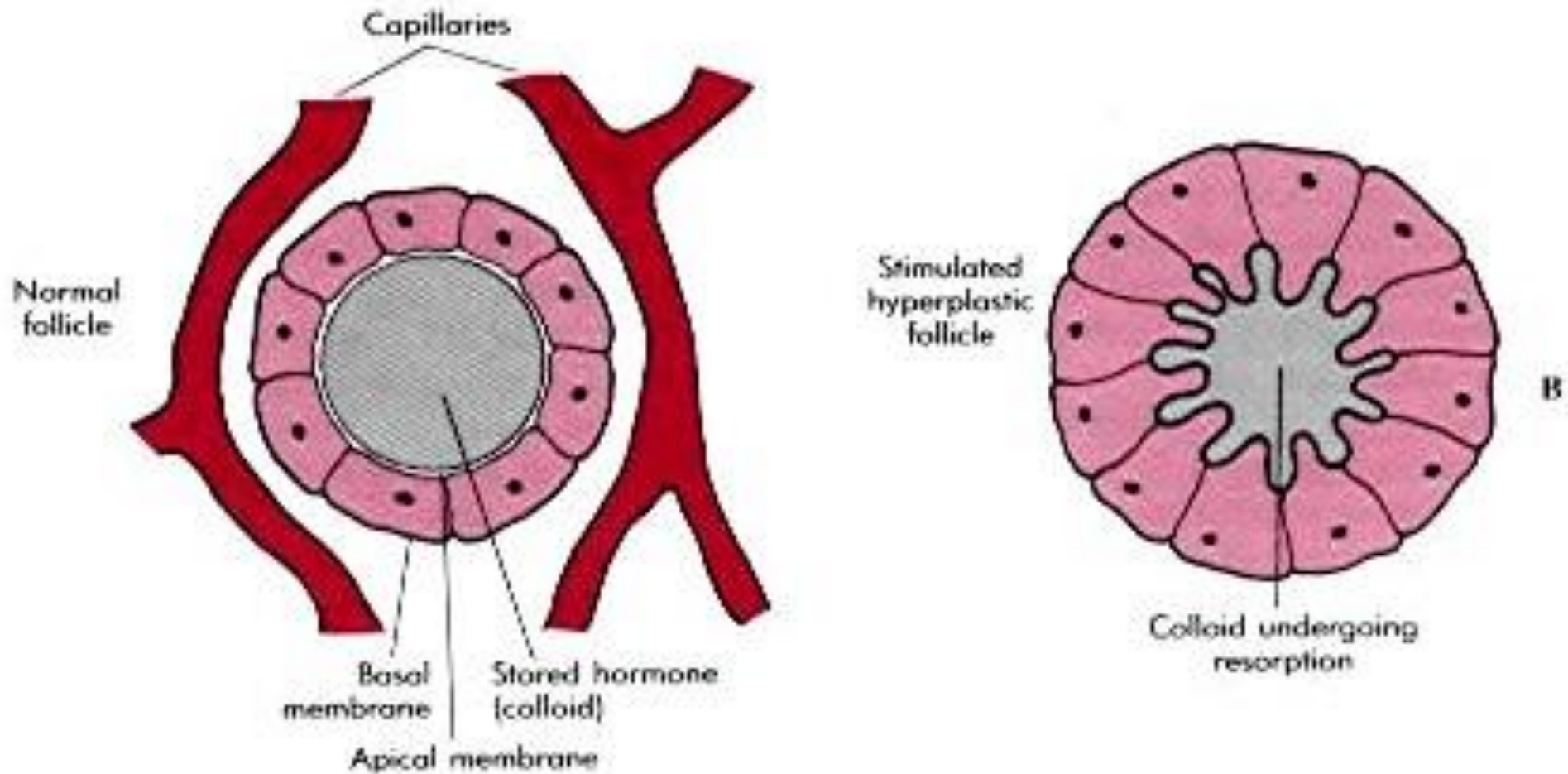
Thyroxine (T₄)



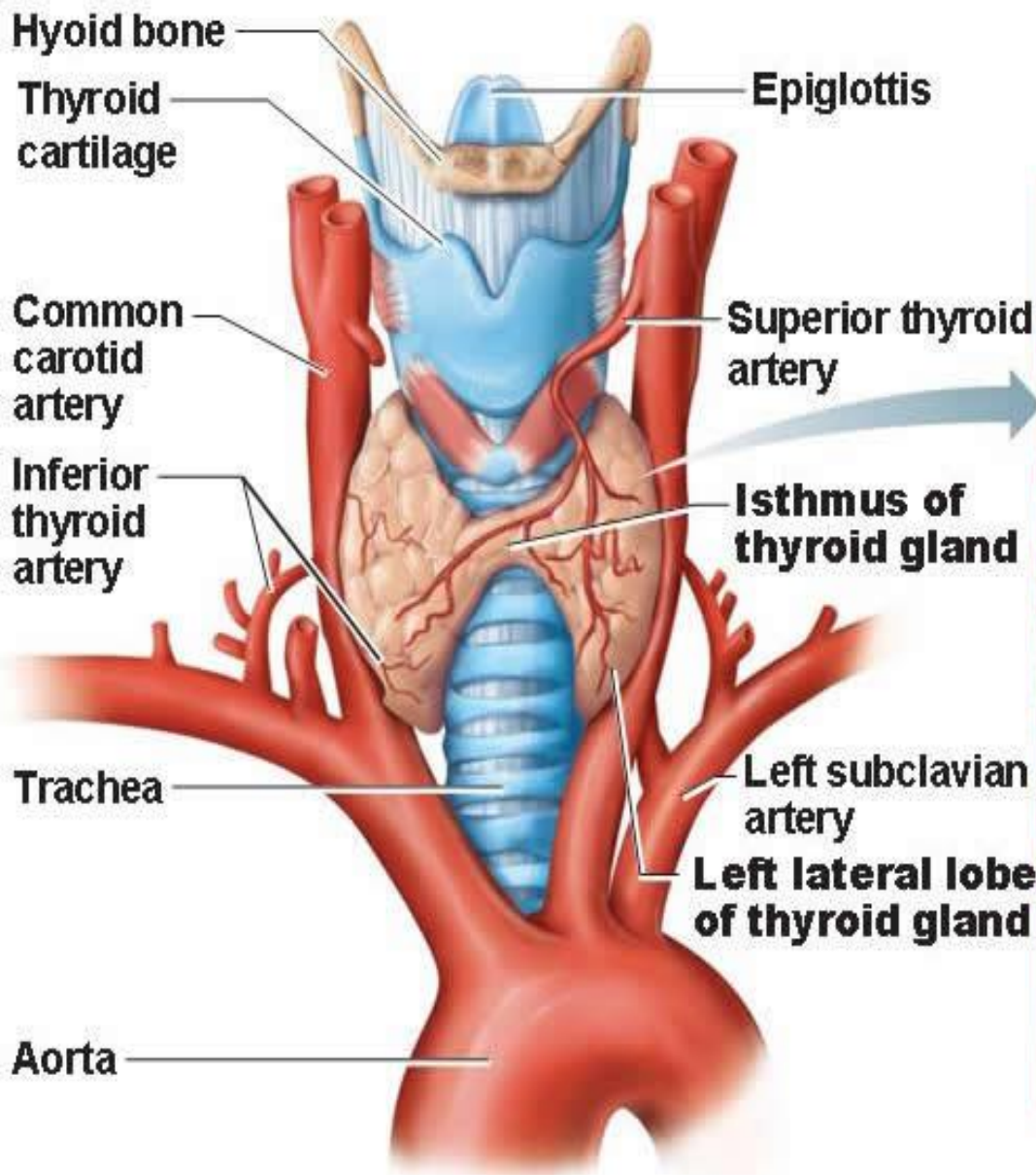
Triiodothyronine (T₃)



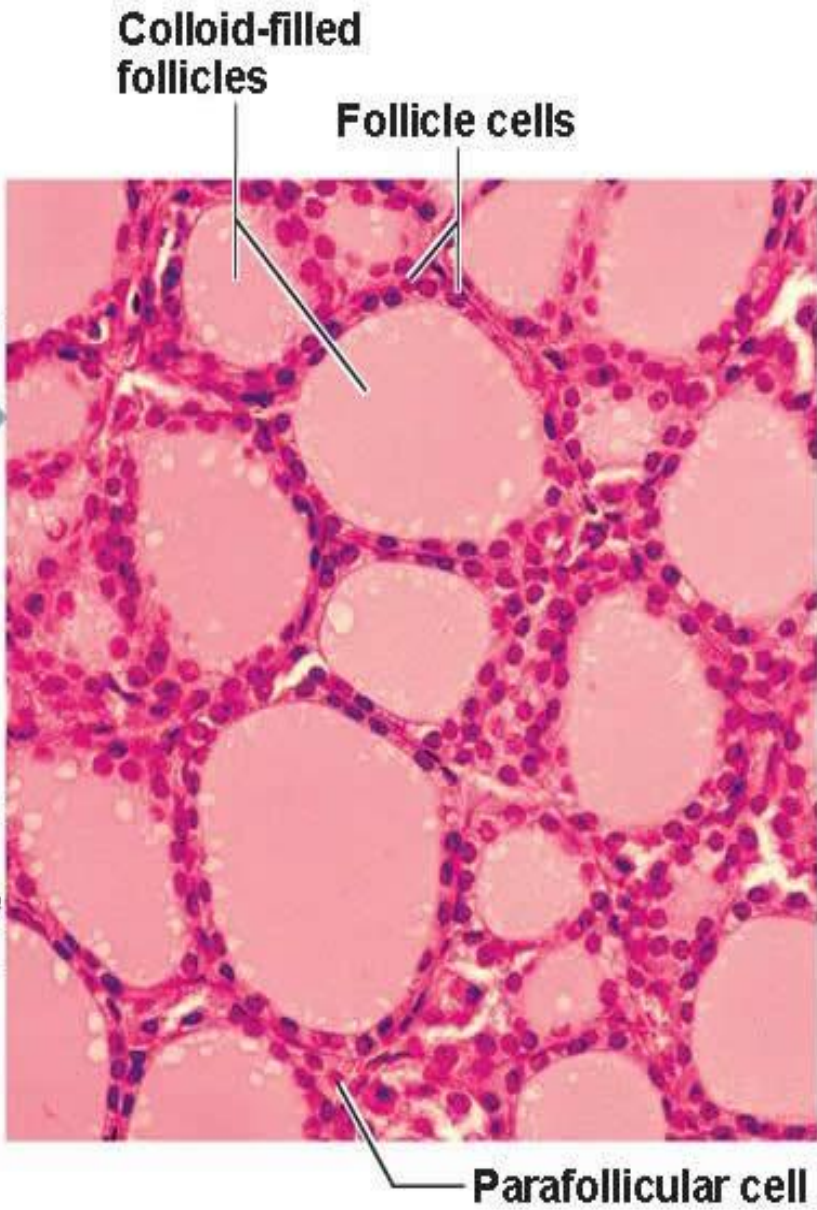
SYNTHESIS



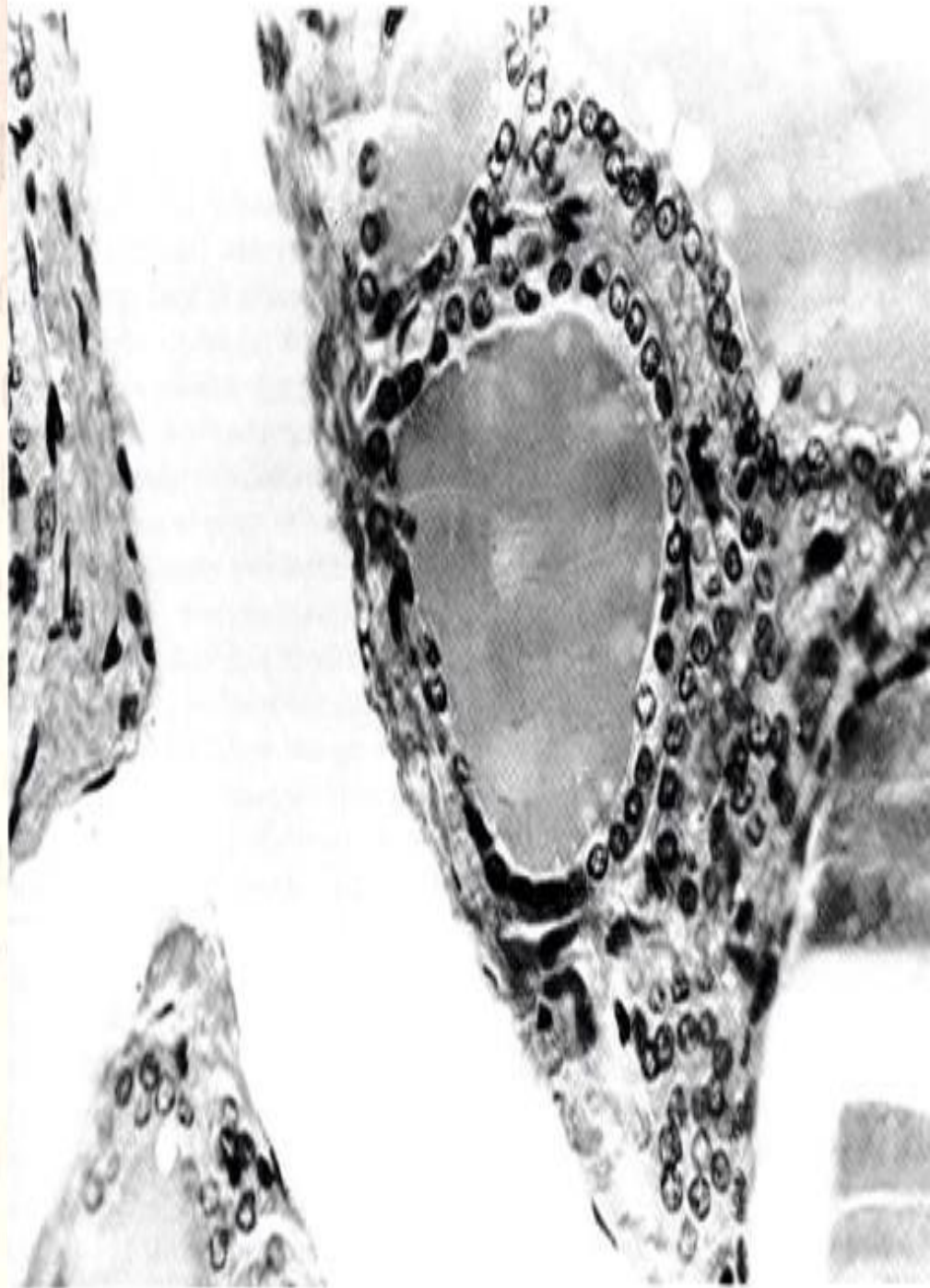
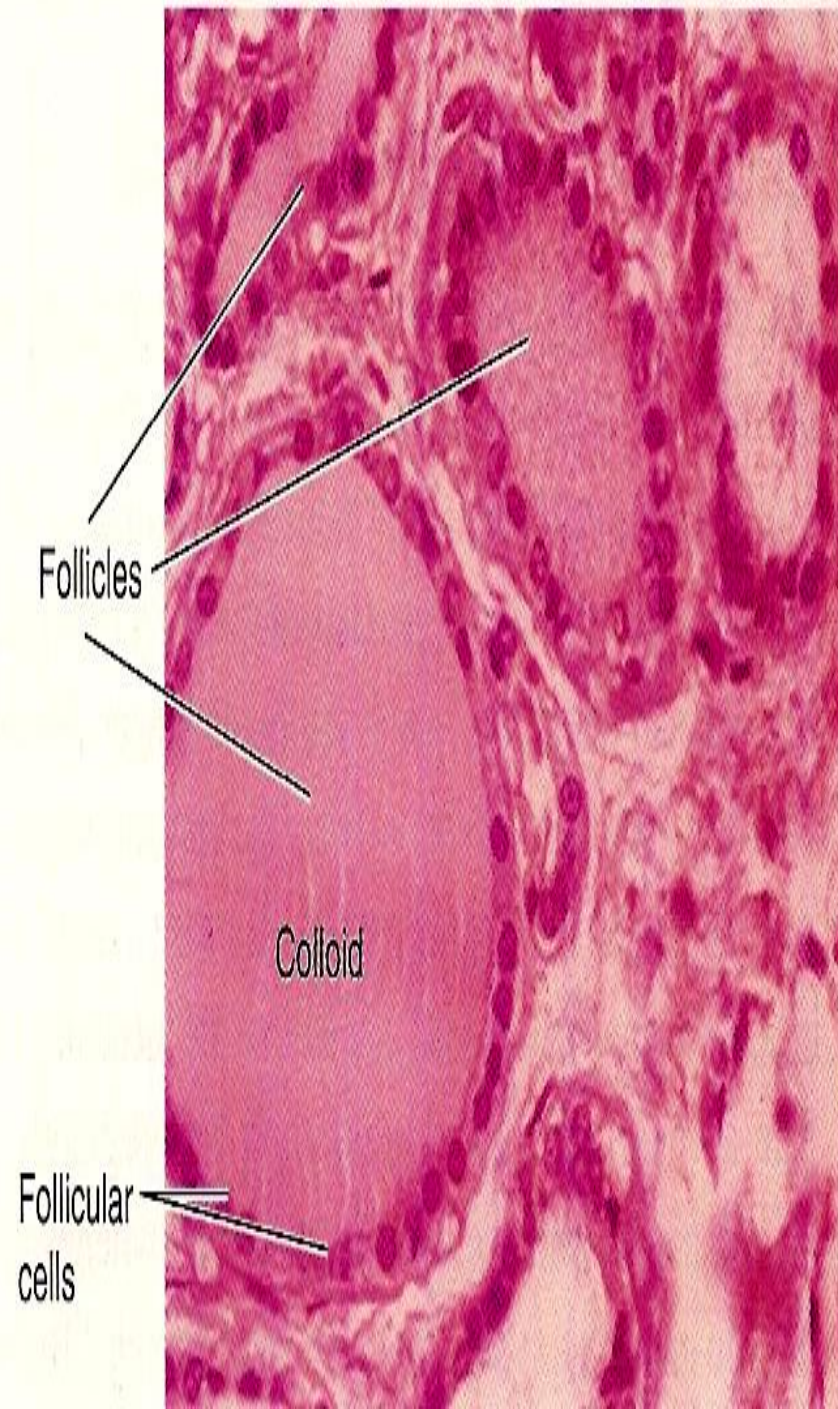
■ Fig. 49-1 A, Photomicrograph of thyroid gland follicle. B, Schematic drawing of normal thyroid gland follicle and a follicle stimulated by thyrotropin. Note change in shapes from cuboidal to columnar, relocation of nuclei to base of cells, and scalloped appearance of follicle lumen.



(a) Gross anatomy of the thyroid gland, anterior view



(b) Photomicrograph of thyroid gland follicles (125x)



THREE UNIQUE FEATURES

1- Contains a large amount of iodine.

- supplied in diet.

- 1mg/week.

2- Synthesis is partially intracellular and partially extracellular.

3- T4 is the major product.

STEPS IN BIOSYNTHESIS

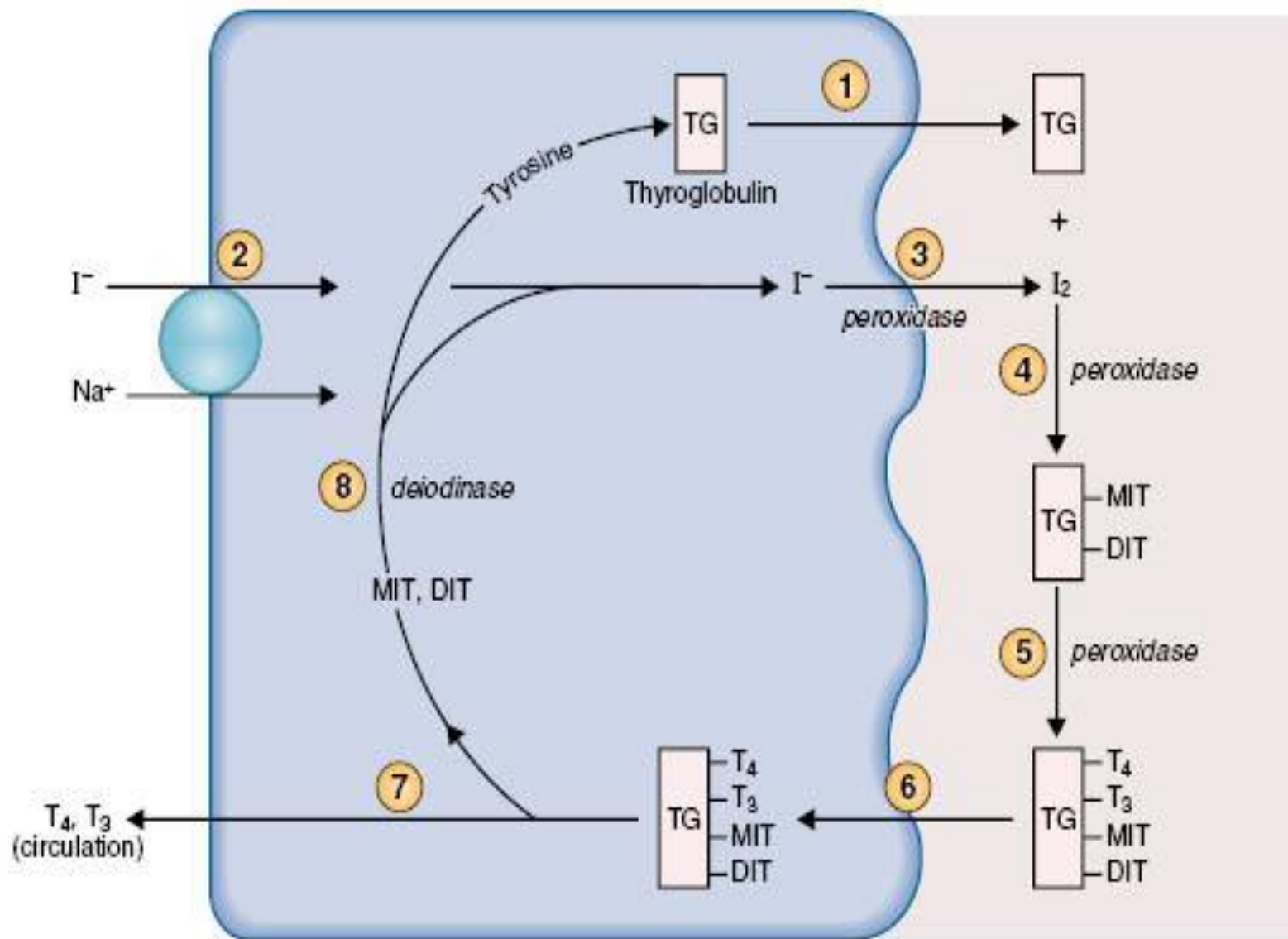
1- THYROGLOBULIN FORMATION AND TRANSPORT:

- 140 tyrosine.**
- Rough endoplasmic reticulum and Golgi apparatus.**

Blood

Follicular epithelial cell

Follicular lumen



2- IODIDE PUMP OR IODIDE TRAP:

- **Active transport**
- **Wolff-chaikoff effect.**
- **Ratio of concentration from 30-250 times.**
- **It is stimulated by TSH.**

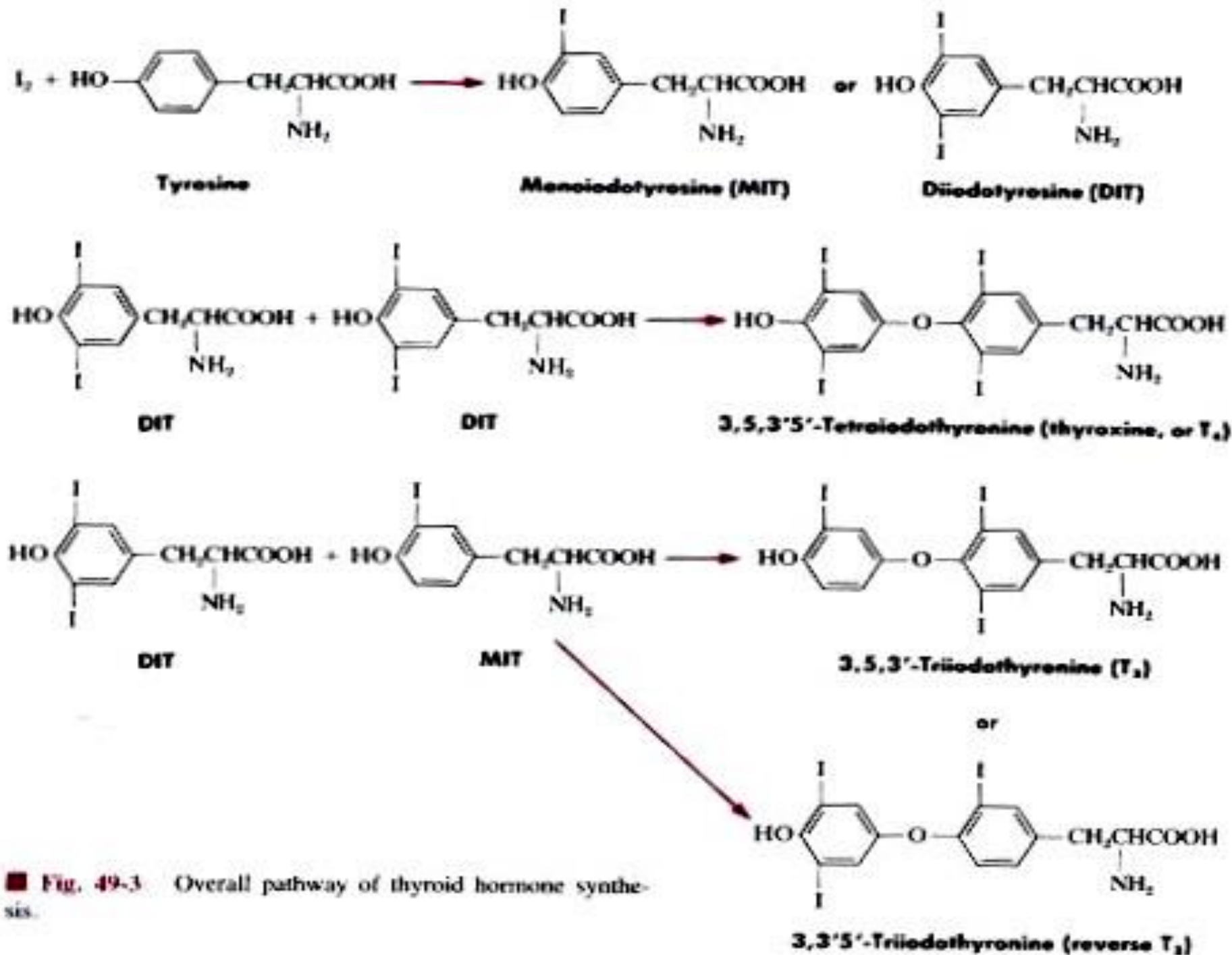
3- OXIDATION OF IODIDE TO IODINE:

- **Thyroid peroxidase.**
- **- It is located in or attached to the apical membrane.**

5- COUPLING REACTION:



- Catalyzed by thyroid peroxidase.
- It is stored as colloid.
- Is sufficient for **2-3 months**.



■ **Fig. 49-3** Overall pathway of thyroid hormone synthesis.

6- Endocytosis of thyroglobulin.

7- Fusion of lysosomes immediately with the vesicles.

8- Hydrolysis of the peptide bond to release *DIT+MIT+T4+T3* from the thyroglobulin.

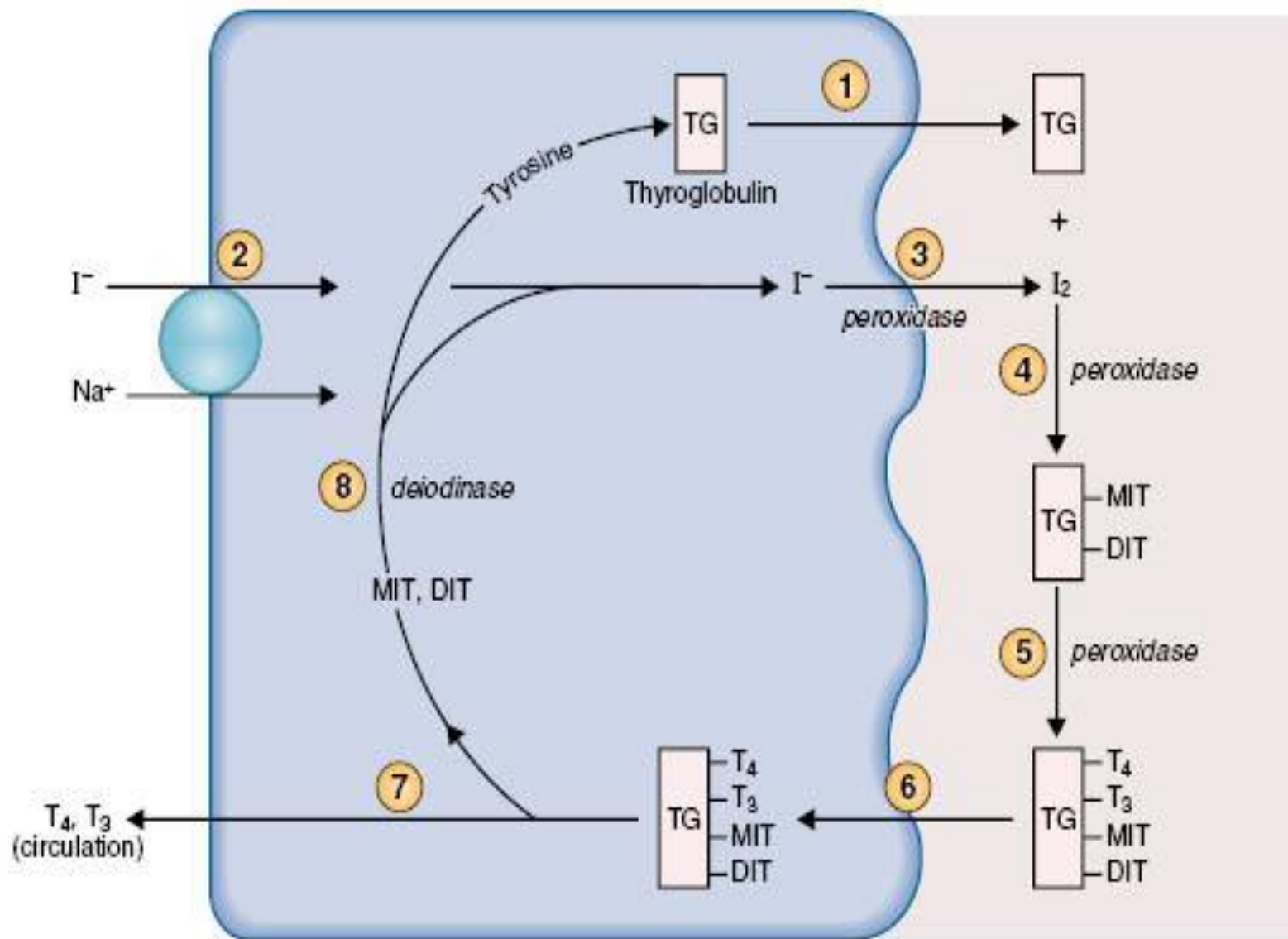
9- Delivery of T₄ and T₃ to the systemic circulation.

10- Deiodination of DIT and MIT by thyroid deiodinase.

Blood

Follicular epithelial cell

Follicular lumen

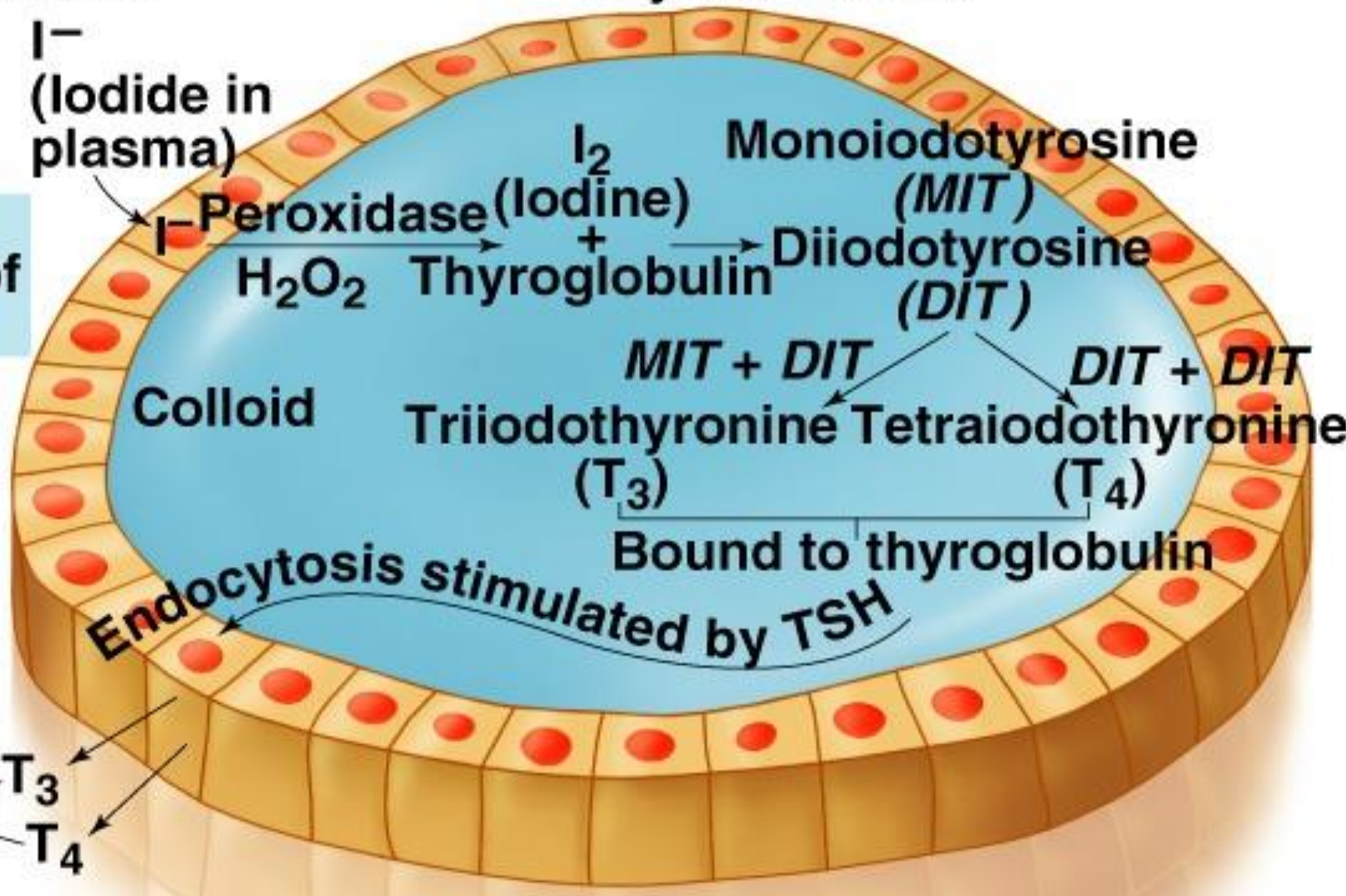


Blood plasma

Thyroid follicle

I⁻
(Iodide in plasma)

Thyroid uptake of iodide



Plasma carrier protein
T₃
T₄

Thyroid hormone secretion

Event	Site	Enzyme	Inhibitor
1 Synthesis of TG; extrusion into follicular lumen	Rough ER, Golgi apparatus		
2 Na ⁺ - I ⁻ cotransport	Basal membrane		Perchlorate, thiocyanate
3 Oxidation of I ⁻ → I ₂	Apical (luminal) membrane	Peroxidase	PTU
4 Organification of I ₂ into MIT and DIT	Apical membrane	Peroxidase	PTU
5 Coupling reaction of MIT and DIT into T ₃ and T ₄	Apical membrane	Peroxidase	PTU
6 Endocytosis of TG	Apical membrane		
7 Hydrolysis of T ₄ and T ₃ ; T ₄ and T ₃ enter circulation	Lysosomes	Proteases	
8 Deiodination of residual MIT and DIT Recycling of I ⁻ and tyrosine	Intracellular	Deiodinase	

THYROID HORMONES IN THE CIRCULATION

1- Unbound:

Small amount

2- Bound:

- 70- 80% bound to thyroxine-binding globulin (TBG) synthesised in the liver.
- The remaining is bound to albumine.

In liver disease:

↓ TBG → ↑ T3 + T4 free level →
inhibition of thyroid secretion.

In pregnancy:

↑ estrogen → ↑ TBG → ↓ T3 + T4
free level → stimulation of
thyroid secretion.

RELEASE OF T4 AND T3 TO THE TISSUES

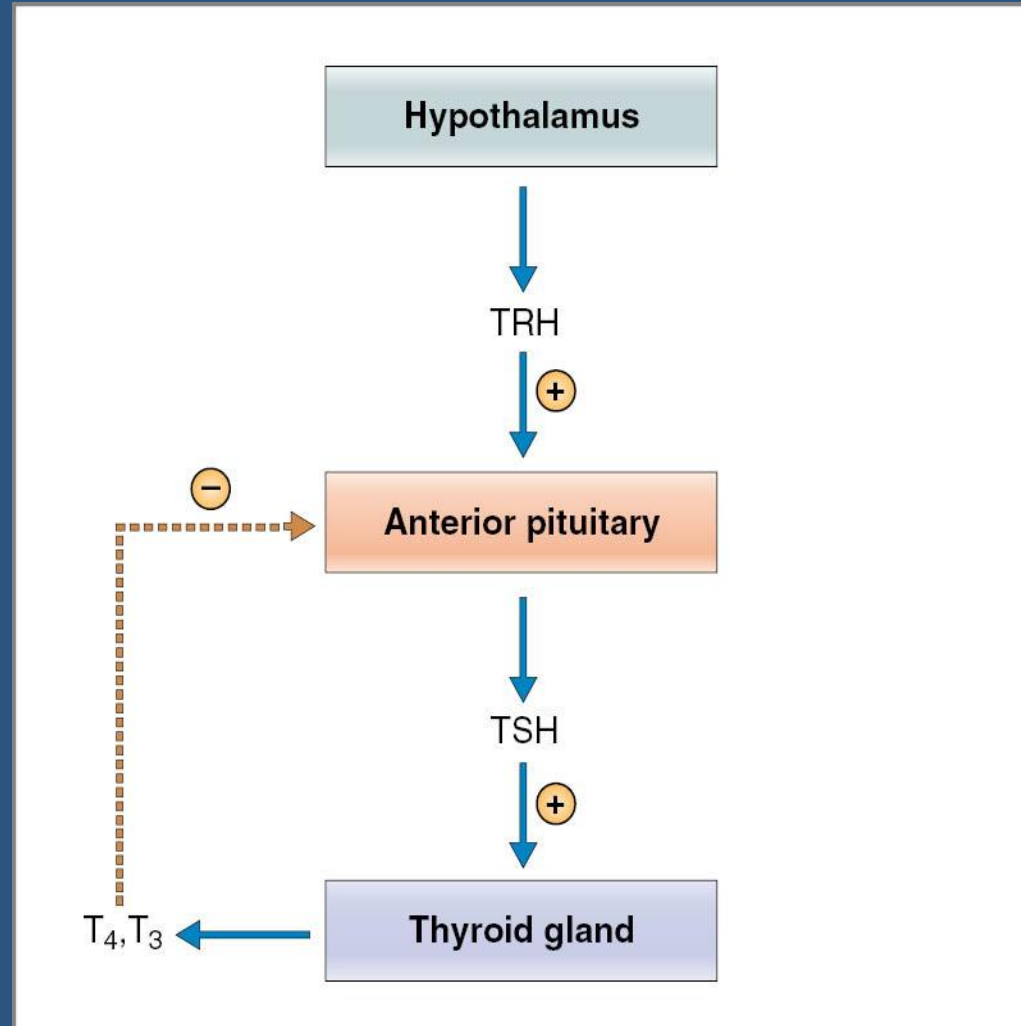
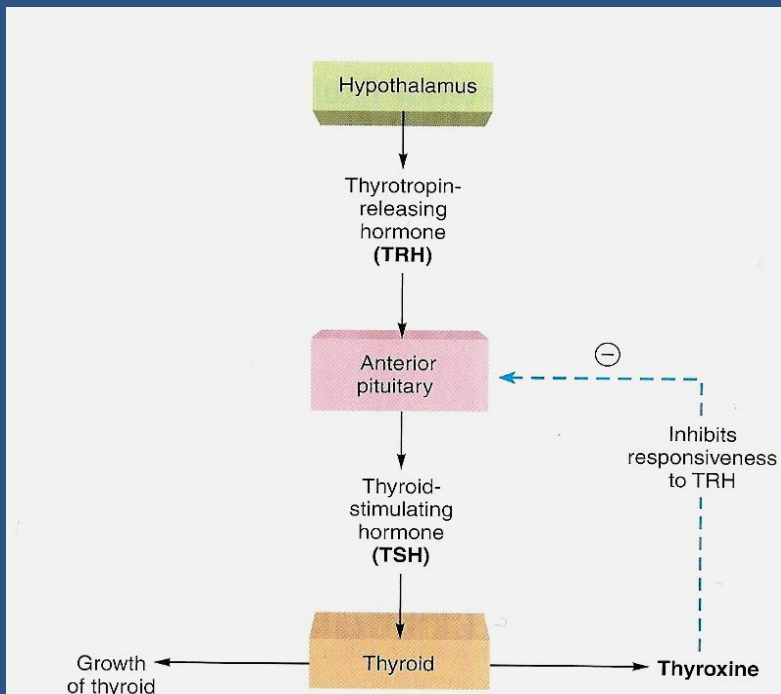
1. The release is slow because of the high affinity of the plasma binding proteins.
 - **$\frac{1}{2}$ of T4** in the blood is released every **6 days**.
 - **$\frac{1}{2}$ of T3** in the blood is released every **one day**.

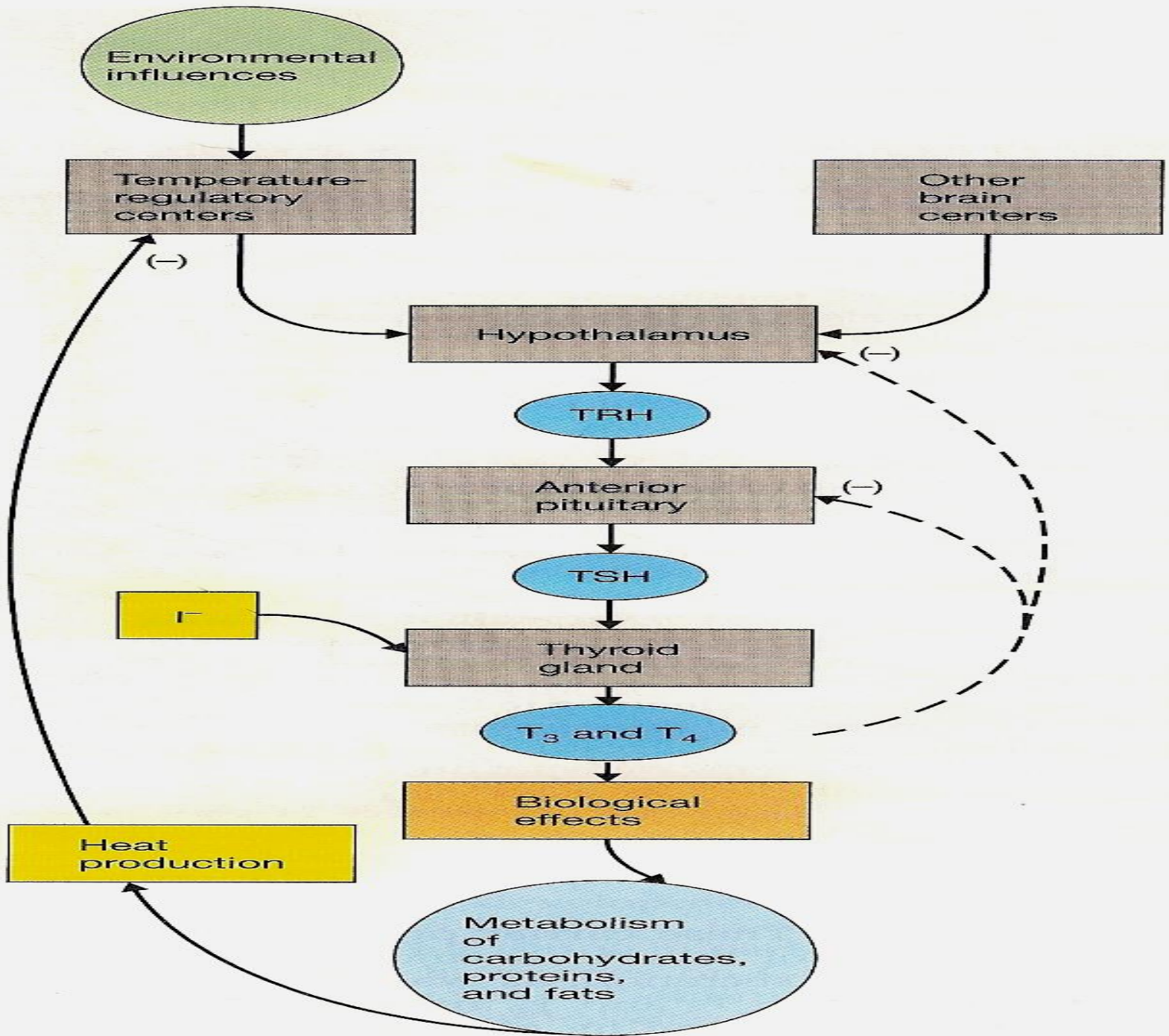
2- Stored in the targeted tissues .

3- Enzyme 5- iodinase.

REGULATION OF HORMONES SECRETION

- It is regulated by the hypothalamic-pituitary axis.





1- Thyrotropin-releasing hormone (TRH):

- Tripeptide.**
- Paraventricular nuclei of the hypothalamus.**
- Act on the thyrotrophs of the anterior pituitary**
- Transcription and secretion of TSH.**

2- Thyroid-stimulating hormone (TSH):

- Glycoprotein.**
- Anterior pituitary.**
- Regulate secretion and growth of thyroid gland (trophic effect).**

Action of TSH

- 1- Increase proteolysis of the thyroglobulin.**
- 2- Increase pump activity.**
- 3- Increase iodination of tyrosine.**
- 4- Increase coupling reaction.**
- 5- Trophic effect.**

- **TSH secretion started at 11-13 of gestational weeks.**
- **TSH + receptor → activation of adenylyl cyclase via Gs protein → ↑cAMP → ↑ activation of protein kinase → multiple phosphorylation → secretion and thyroid growth.**

Table 9-8 Factors Affecting Thyroid Hormone Secretion

Stimulatory Factors

TSH

Thyroid-stimulating immunoglobulins

Increased TBG levels (e.g., pregnancy)

Inhibitory Factors

I⁻ deficiency

Deiodinase deficiency

Excessive I⁻ intake (Wolff-Chaikoff effect)

Perchlorate; thiocyanate (inhibit Na⁺-I⁻ cotransport)

Propylthiouracil (inhibits peroxidase enzyme)

Decreased TBG levels (e.g., liver disease)

ACTION OF THYROID HORMONES

- Before binding to the nuclear receptors **90% of T4 is converted to T3.**

T3 + nuclear receptor → T3-receptor complex →
activation of thyroid regulating element on DNA →
DNA transcription → formation of mRNA →
translation of mRNA → specific protein
synthesis (target tissue specific).

1- Basal metabolic rate (BMR):

- Is the energy requirement under basal condition (state of mental and physical rest 12-18 hours after a meal).**
- Complete lack of thyroid hormones → ↓ 40% in BMR.**
- Extreme increase of thyroid hormones → ↑ 60-100% in BMR.**

2- Metabolism

A)- Effect on carbohydrate metabolism:

- 1- Increase glucose uptake by the cells.
- 2- Increase **glycogenolysis**.
- 3- Increase **gluconeogenesis**.
- 4- Increase absorption from the gastrointestinal tract.

B)- Effects on fat metabolism:

- 1- Increase lipolysis.**
- 2- Decrease plasma cholesterol by increase loss in feces.**
- 3- Increase oxidation of free fatty acids.**

C)- Effect on protein metabolism:

overall effect is catabolic leading to decrease in muscle mass.

3- Effects on the cardiovascular system:

- Increase heart rate. Cardiac out put up to 60%
- Increase stroke volume.
- Decrease peripheral resistance.

end result is increase delivery of **oxygenated** blood to the tissues.

1- Thyroid hormones potentiate the effect of catecholamine in the circulation —→ activation of β -adrenergic receptors.

2- Direct induction of:

a)- myocardial β -adrenergic receptors.

b)- sarcoplasmic reticulum.

c)- Ca^{+2} ATPase.

6- Effects on the CNS:

A)- fetal and postnatal life

Thyroid hormones are essential for maturation of the CNS.

perinatal decrease of hormones secretion



mental retardation

- Screening is necessary to introduce hormone replacement .**

B)- In adult:

Increase in thyroid hormone secretion:

- 1-Hyperexcitability.**
- 2- Irritability.**

Decrease in thyroid hormones secretion:

- 1- Slow movement.**
- 2- Impaired memory.**
- 3-[↓] Mental capacity.**

7- Effects on Autonomic nervous system:

Produced the same action as catecholamine's via

β -adrenergic receptors including:

- a)- increase BMR.
- b)- increase heat production.
- c)- increase heart rate.
- d)- increase stroke volume.

i.e. β -blocker (propranolol) is used in treatment of hyperthyroidism.

8- Effects on bone:

- a)- Promote bone formation.**
- b)- Promote ossification.**
- c)- Promote fusion of bone plate.**
- d)- Promote bone maturation.**

9- Effects on respiration:

1- Increase ventilation rate.

2- Increase dissociation of oxygen from Hb by increasing red cells 2,3-DPG (2,3 diphosphoglycerate).

10- Effects on the G.I tract:

1- Increase appetite and food intake.

2- Increase of digestive juices secretion.

3- Increase of G.I tract motility.

excess secretion → diarrhea.

lack of secretion → constipation.

ACTIONS OF THYROID HORMONES

