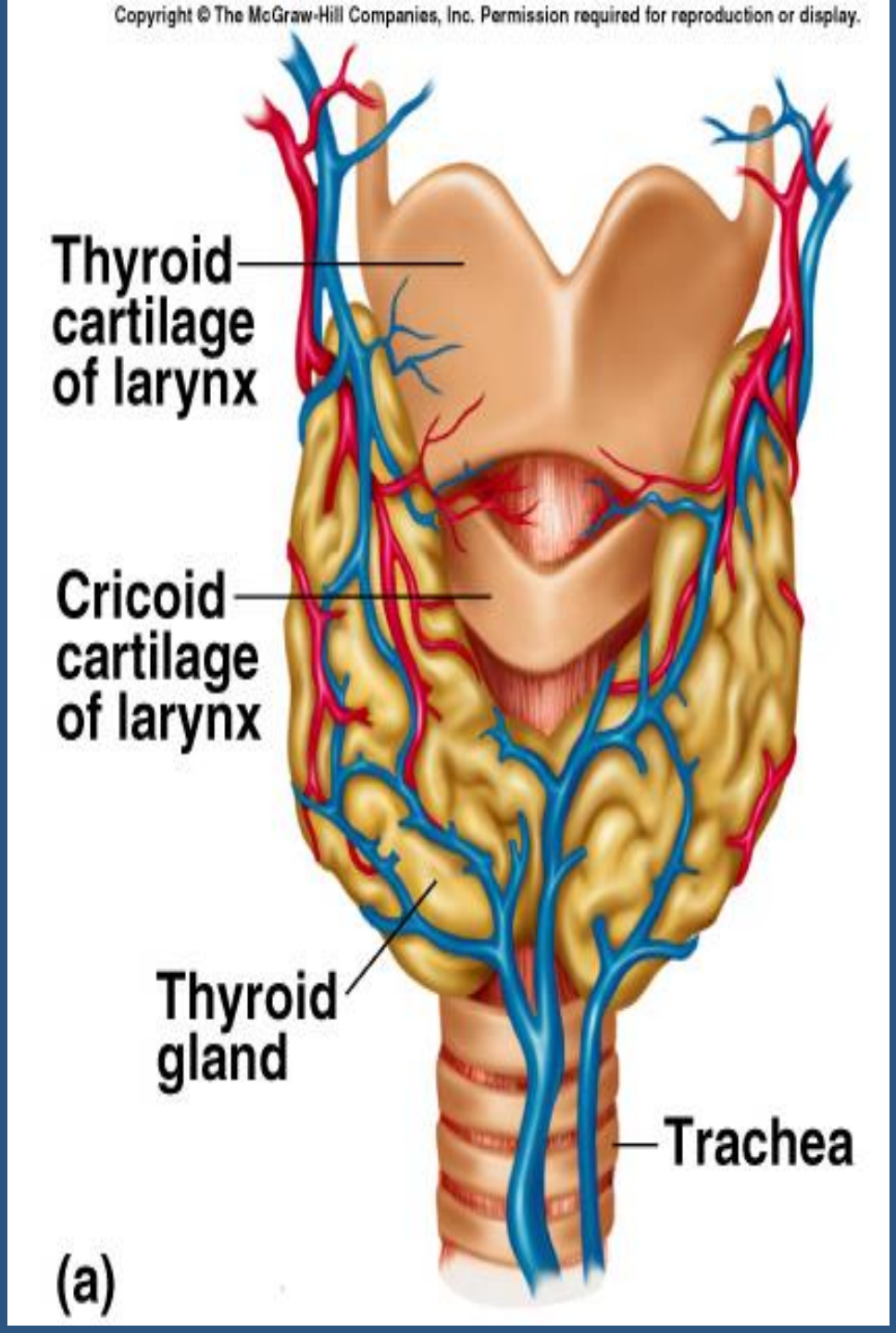
THE THYROID GLAND

PROF. ABDULMAJEED AL-DREES

OBJECTIVES

- LIST THYROID GLAND HORMONES
- DESCRIBE THE SYNTHYSIS OF THE THYROID HORMONES
- DESCRIBE THE RELEASE AND ACTIONSOF THYROID HORMONES
- DESCRIB THE NEGATIVE FEEDBACK MECHANISME (CONTROL)

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



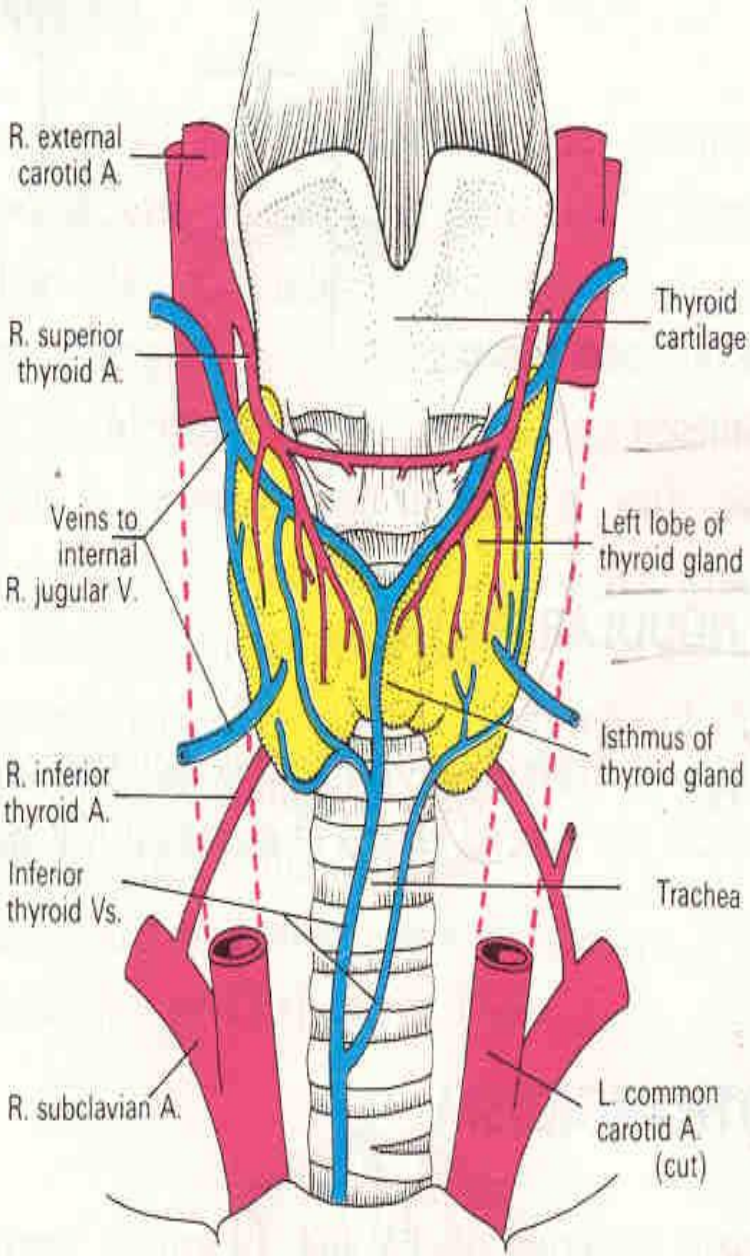
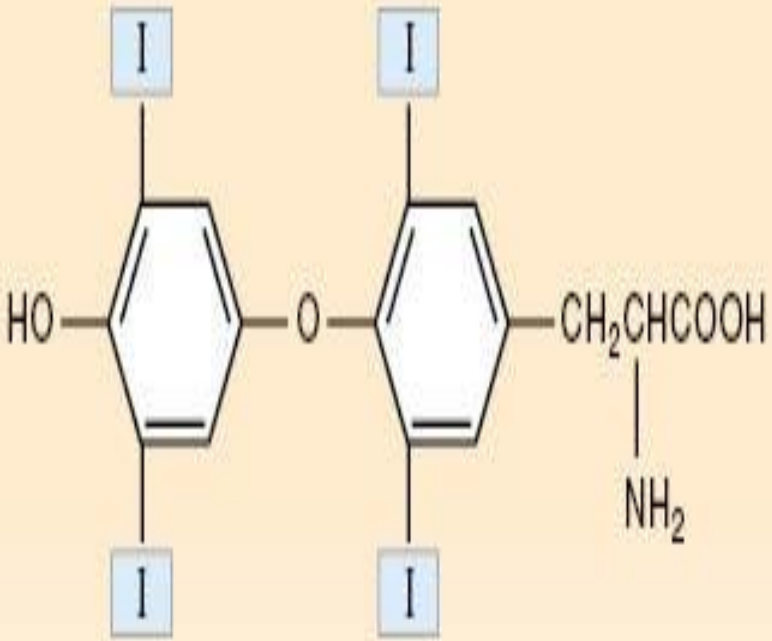


Figure 14:8 Position of thyroid gland and associated structures.

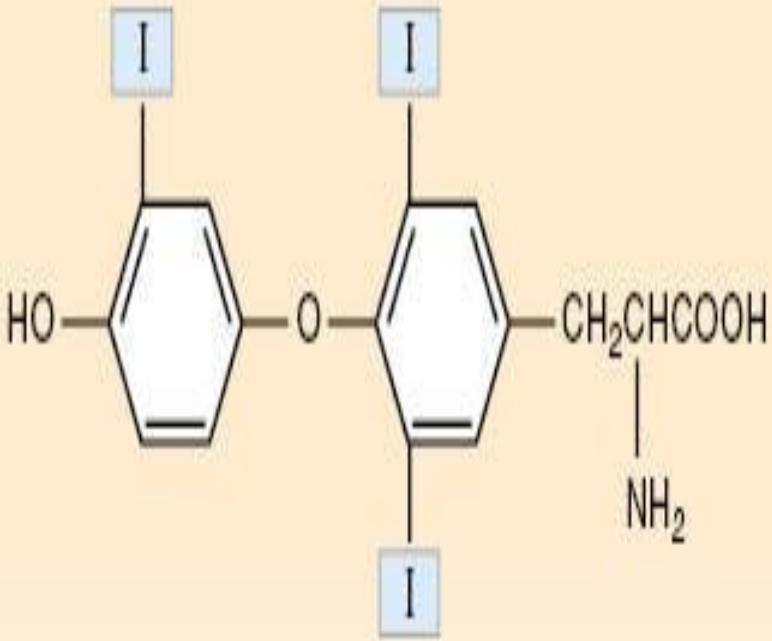
HORMONES

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

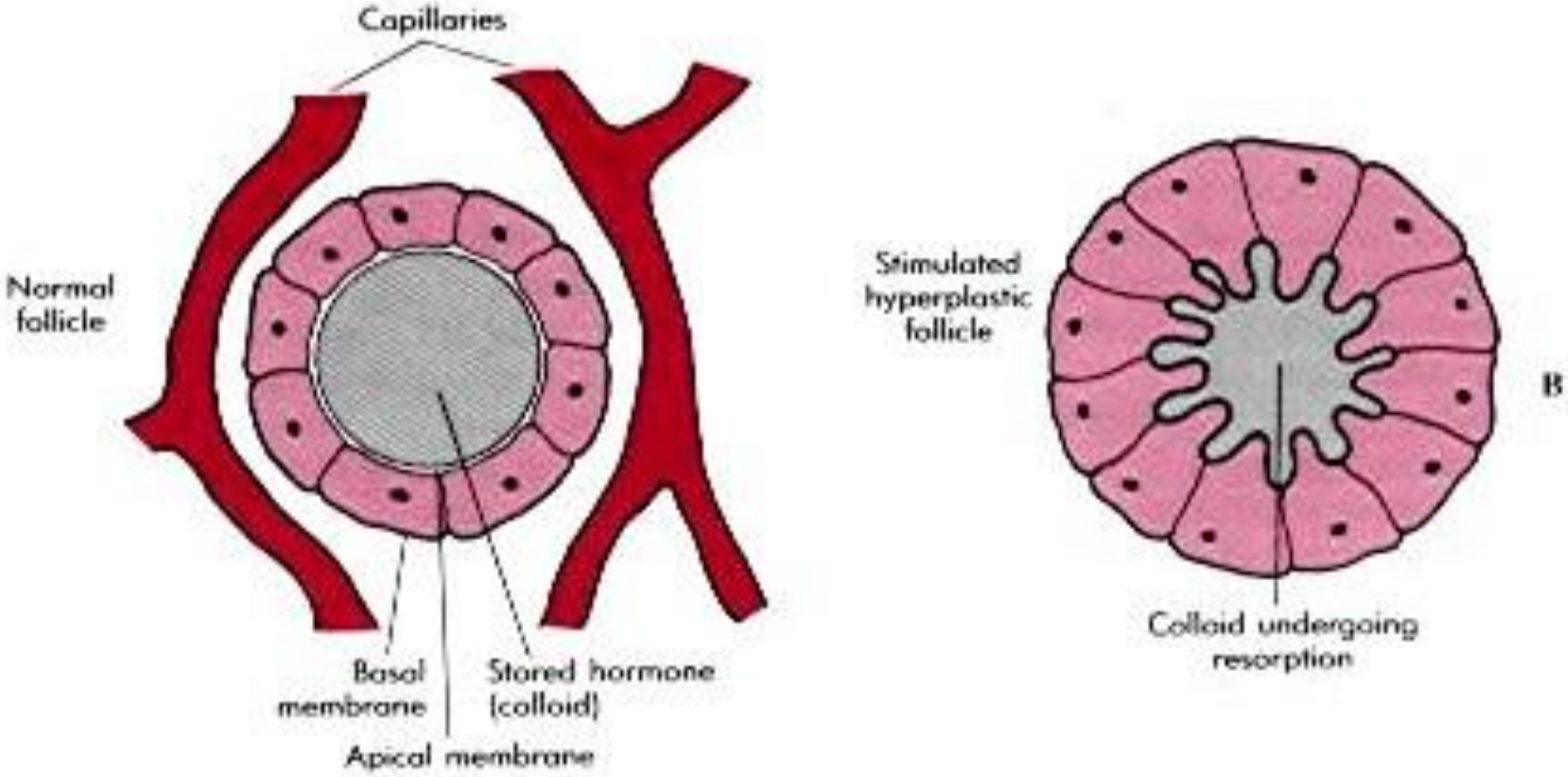
Thyroxine (T_4)



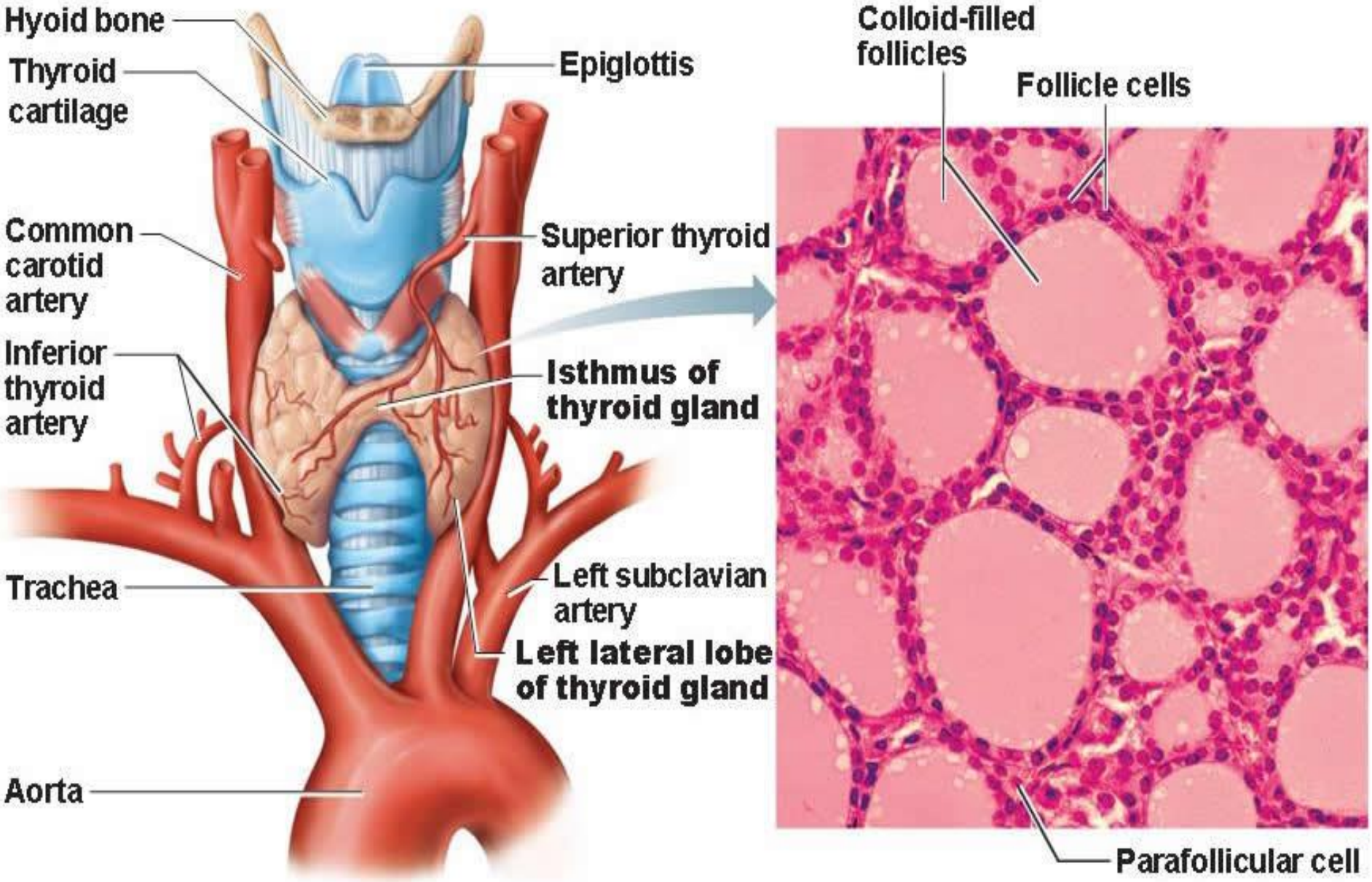
Triiodothyronine (T_3)



SYNTHESIS

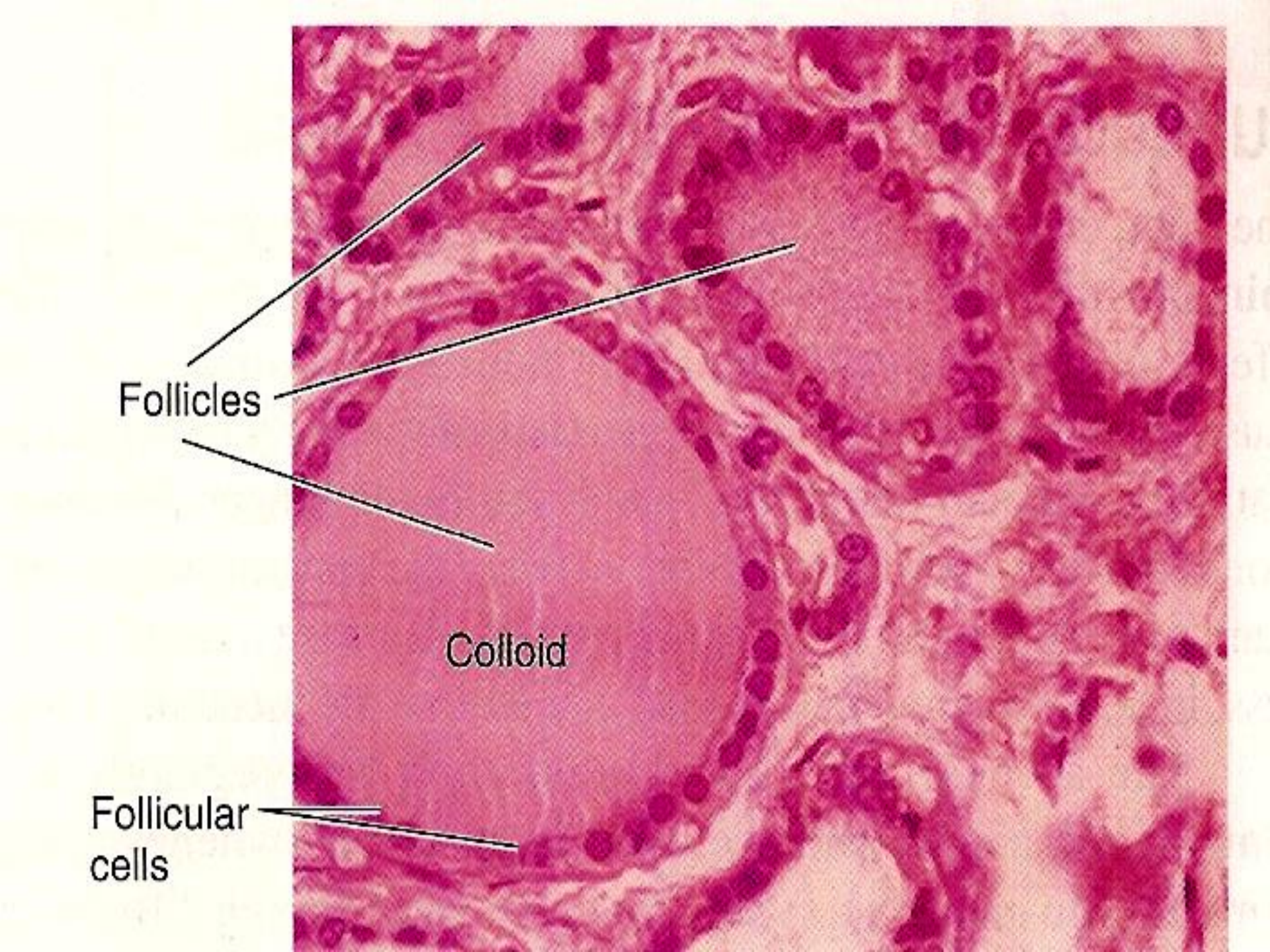


■ Fig. 49-1 **A,** Photomicrograph of thyroid gland follicle. **B,** Schematic drawing of normal thyroid gland follicle and a follicle stimulated by thyrotropin. Note change in shapes from cuboidal to columnar, relocation of nuclei to base of cells, and scalloped appearance of follicle lumen.



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

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


Follicles
Colloid
Follicular cells

THREE UNIQUE FEATURES

1- Contains a large amount of iodine.

- **supplied in diet.**

- **1mg/week.**

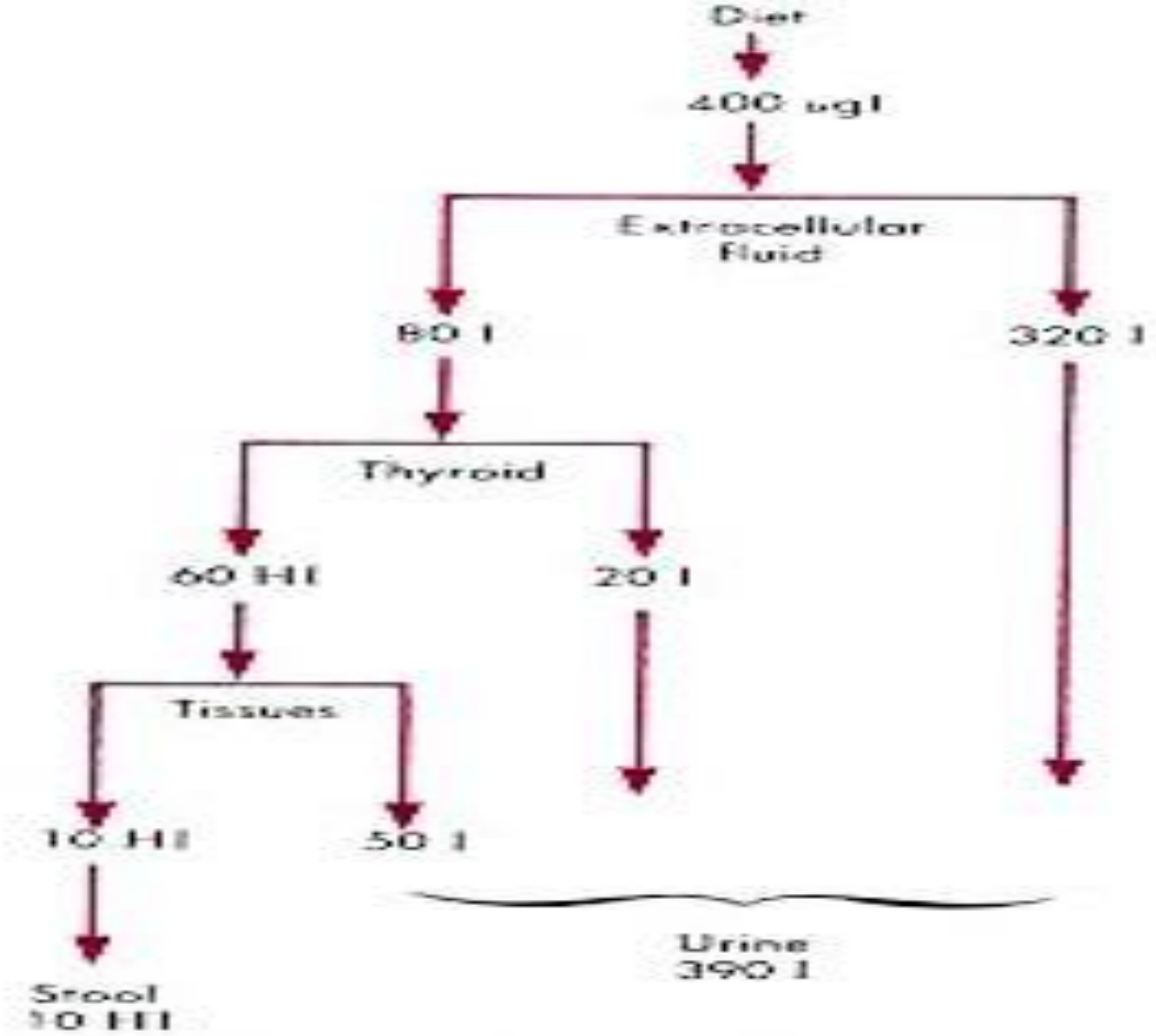


Fig. 49-2 Average daily iodide turnover in humans (United States). Note that 20% of the intake is taken up by the thyroid gland and 15% turns over in hormone synthesis and disposal. The unneeded excess is excreted in the urine. *I*, Iodide; *HI*, hormonal iodide.

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.

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.

4- ORGANIFICATION OF THYROGLOBULIN

- Binding of iodine with Thyroglobulin.
- - Catalyzed by thyroid peroxidase.
  MIT DIT
- - Remain attached to thyroglobulin until the gland stimulated to secret.

5- COUPLING REACTION:

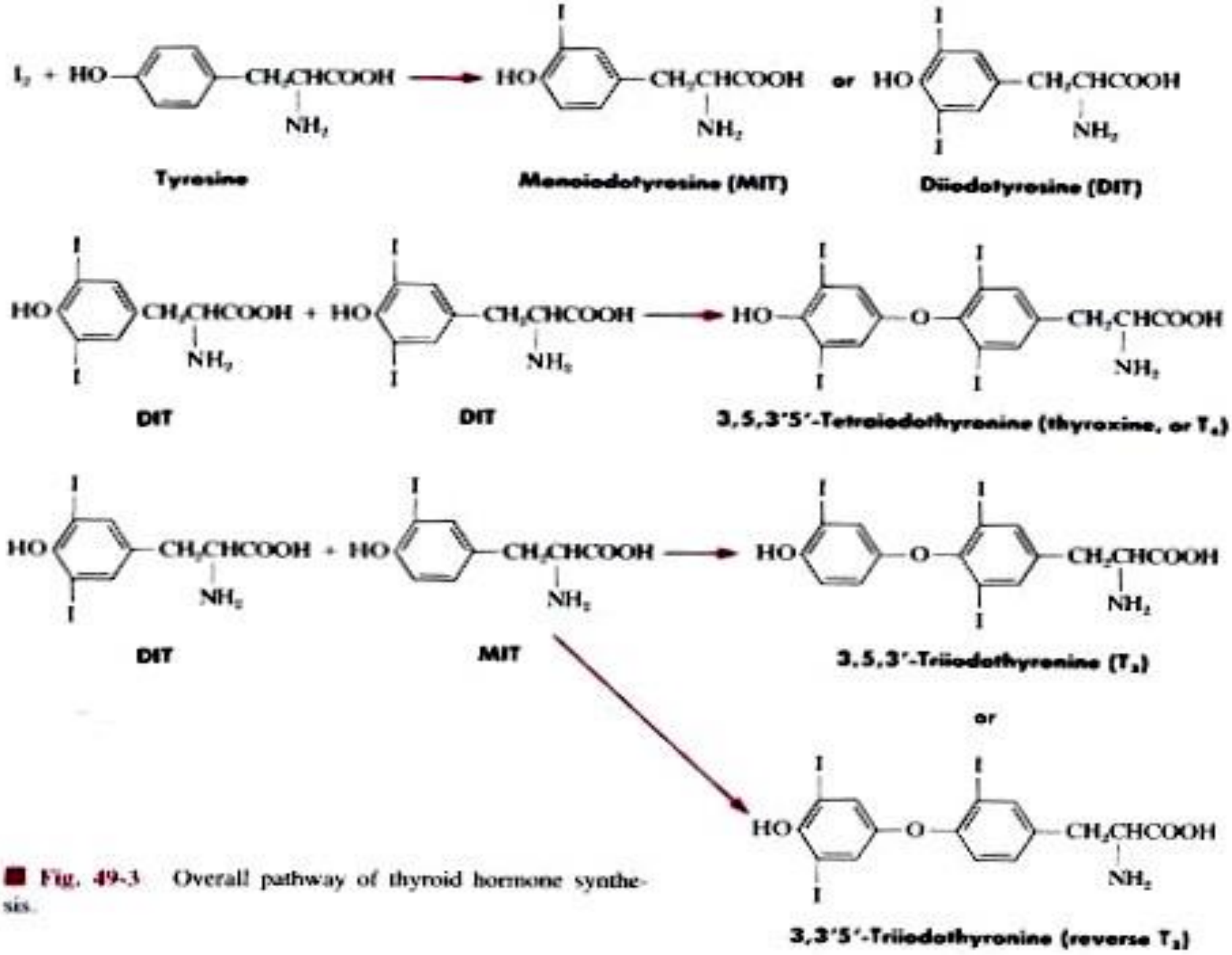
DIT + DIT → T_4 (faster)

DIT + MIT → T_3

- Catalyzed by thyroid peroxidase.

- It is stored as colloid.

- Is sufficient for **2-3 months.**



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

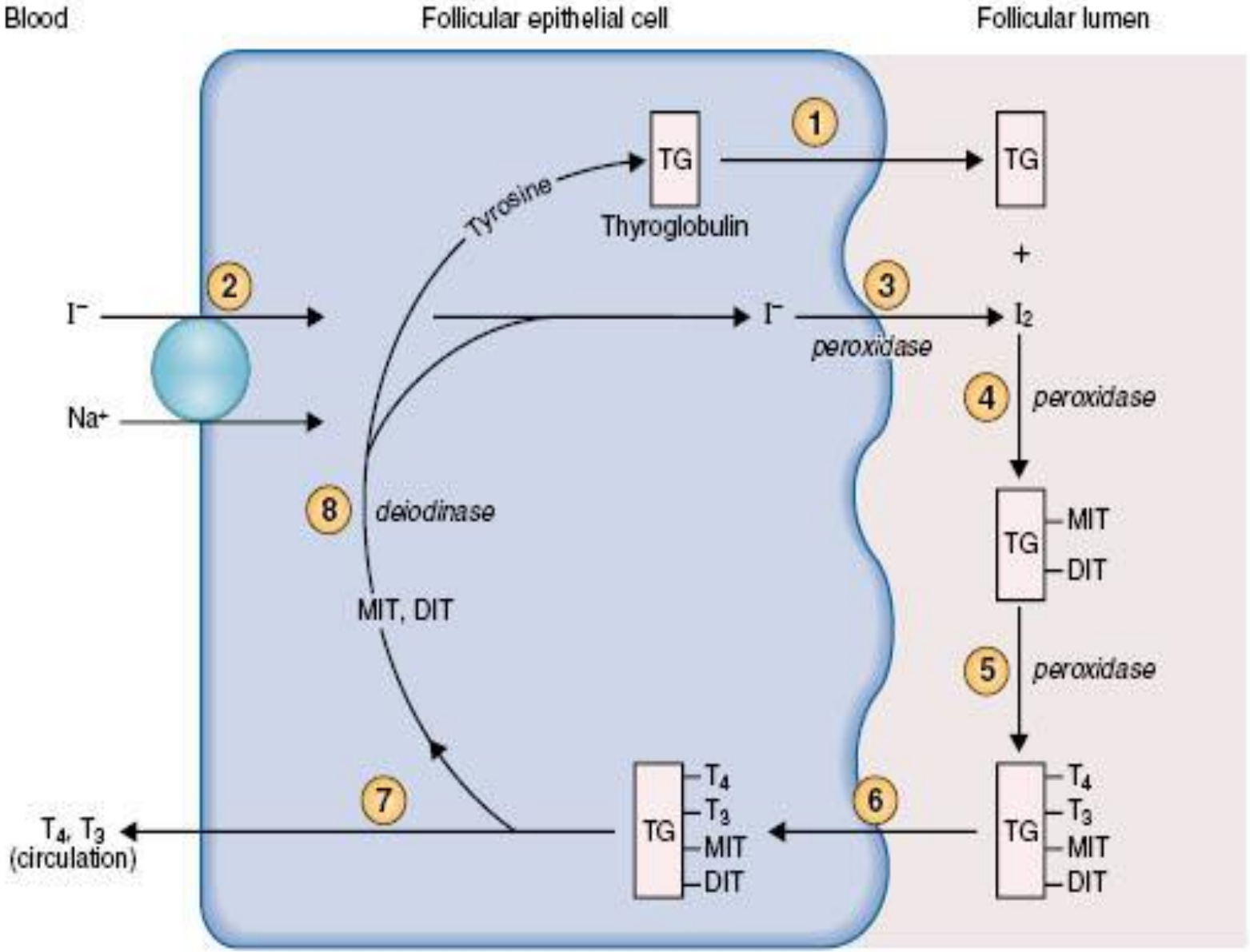
6- Endocytosis of thyroglobulin.

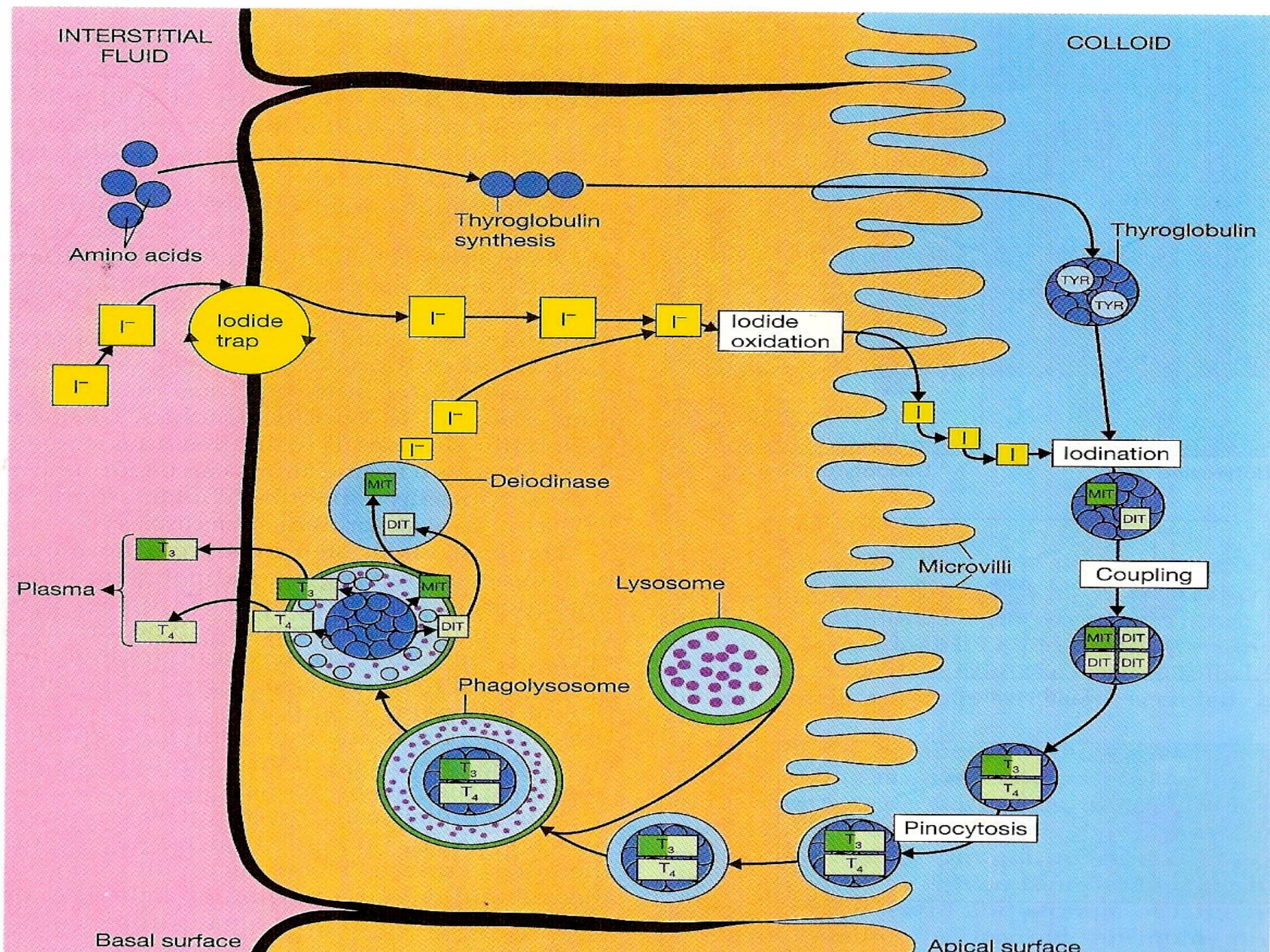
7- Fusion of lysosomes immediately with the vesicles.

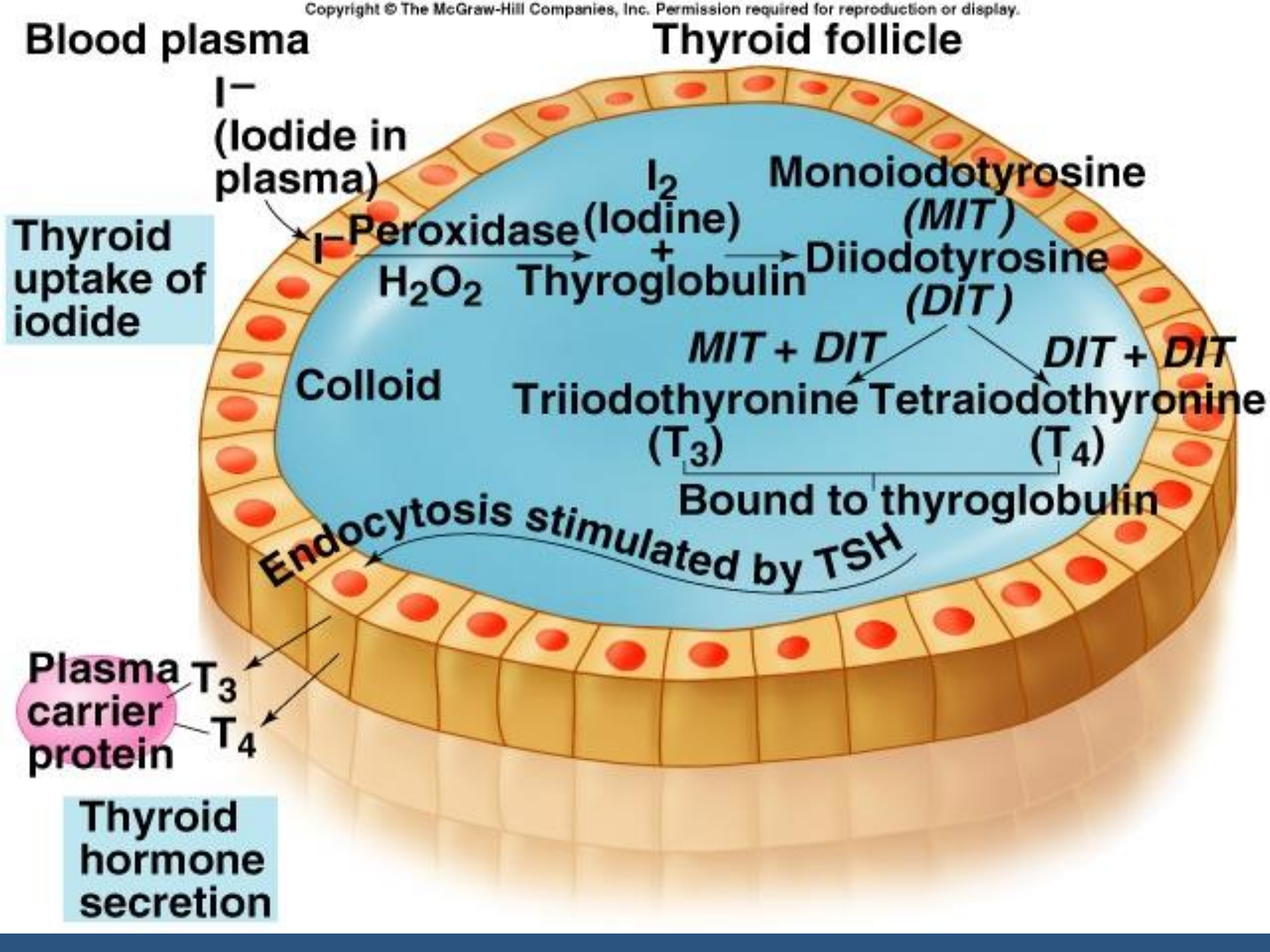
8- Hydrolysis of the peptide bond to release *DIT+MIT+T4+T3* from the thyroglobulin.

9- Delivery of T_4 and T_3 to the systemic circulation.

10- Deiodination of DIT and MIT by thyroid deiodinase.


Blood
Follicular epithelial cell
Follicular lumen
TG
Thyroglobulin
Tyrosine
1
TG
+
2
I⁻
3
I⁻
I₂
peroxidase
Na⁺
4
peroxidase
8
deiodinase
TG
MIT
DIT
MIT, DIT
5
peroxidase
7
6
T4
T3
MIT
DIT
T4, T3
(circulation)
TG
T4
T3
MIT
DIT
TG
T4
T3
MIT
DIT


INTERSTITIAL FLUID
COLLOID
Amino acids
Thyroglobulin synthesis
Thyroglobulin
TYR
TYR
I⁻
I⁻
Iodide trap
I⁻
I⁻
I⁻
Iodide oxidation
I
I
I
Iodination
I⁻
I⁻
MIT
DIT
Deiodinase
MIT
DIT
Microvilli
Coupling
MIT
DIT
DIT
DIT
T3
T4
Plasma
T3
T4
MIT
DIT
Lysosome
Phagolysosome
T3
T4
T3
T4
T3
T4
T3
T4
Pinocytosis
Basal surface
Apical surface



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 $I^- \rightarrow I_2$	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 reminder 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.**

   - ½ of T4 in the blood is released every 6 days.

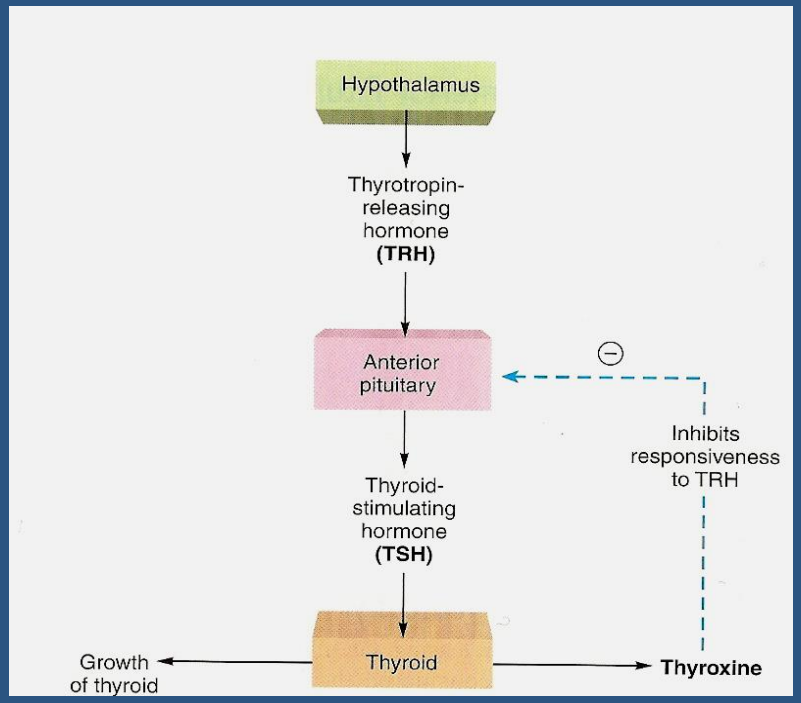
   - ½ of T3 in the blood is released every one day.

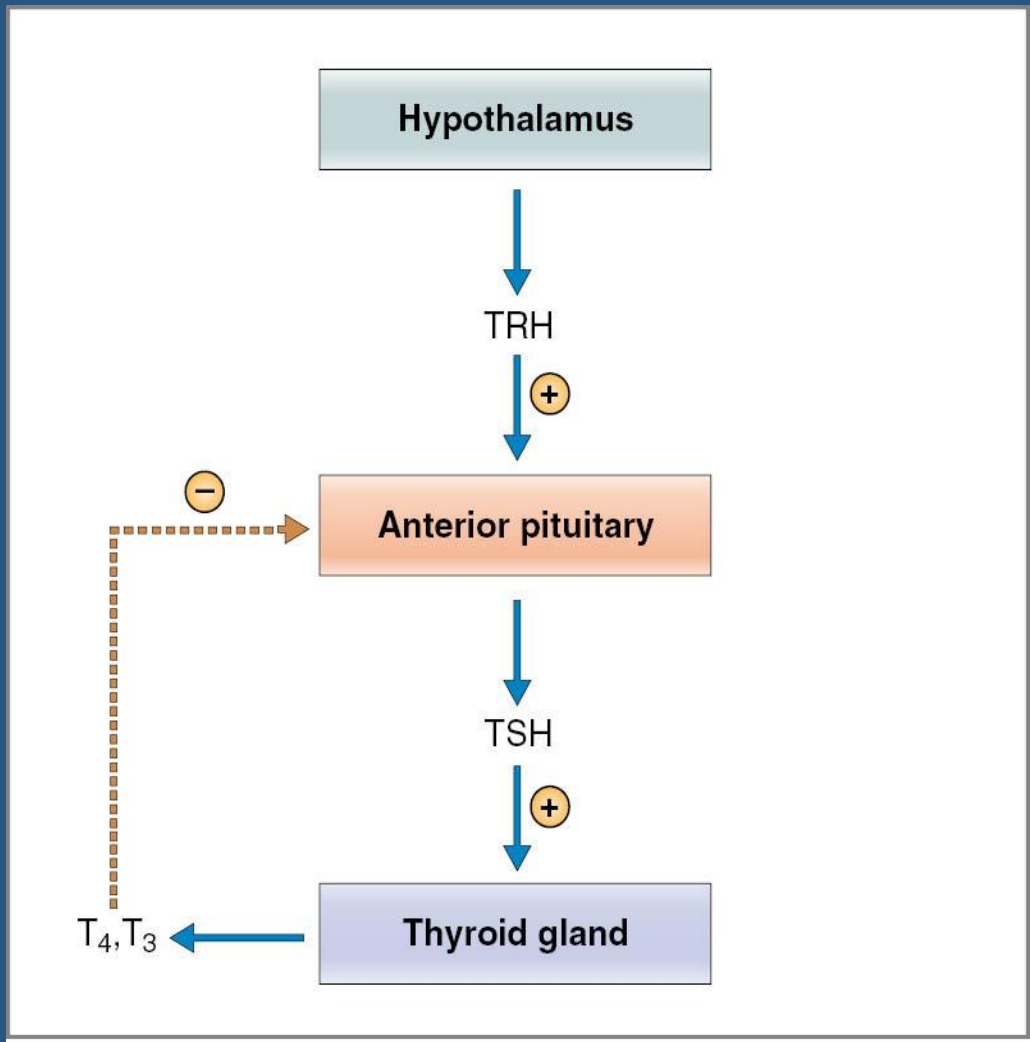
2- Stored in the targeted tissues .

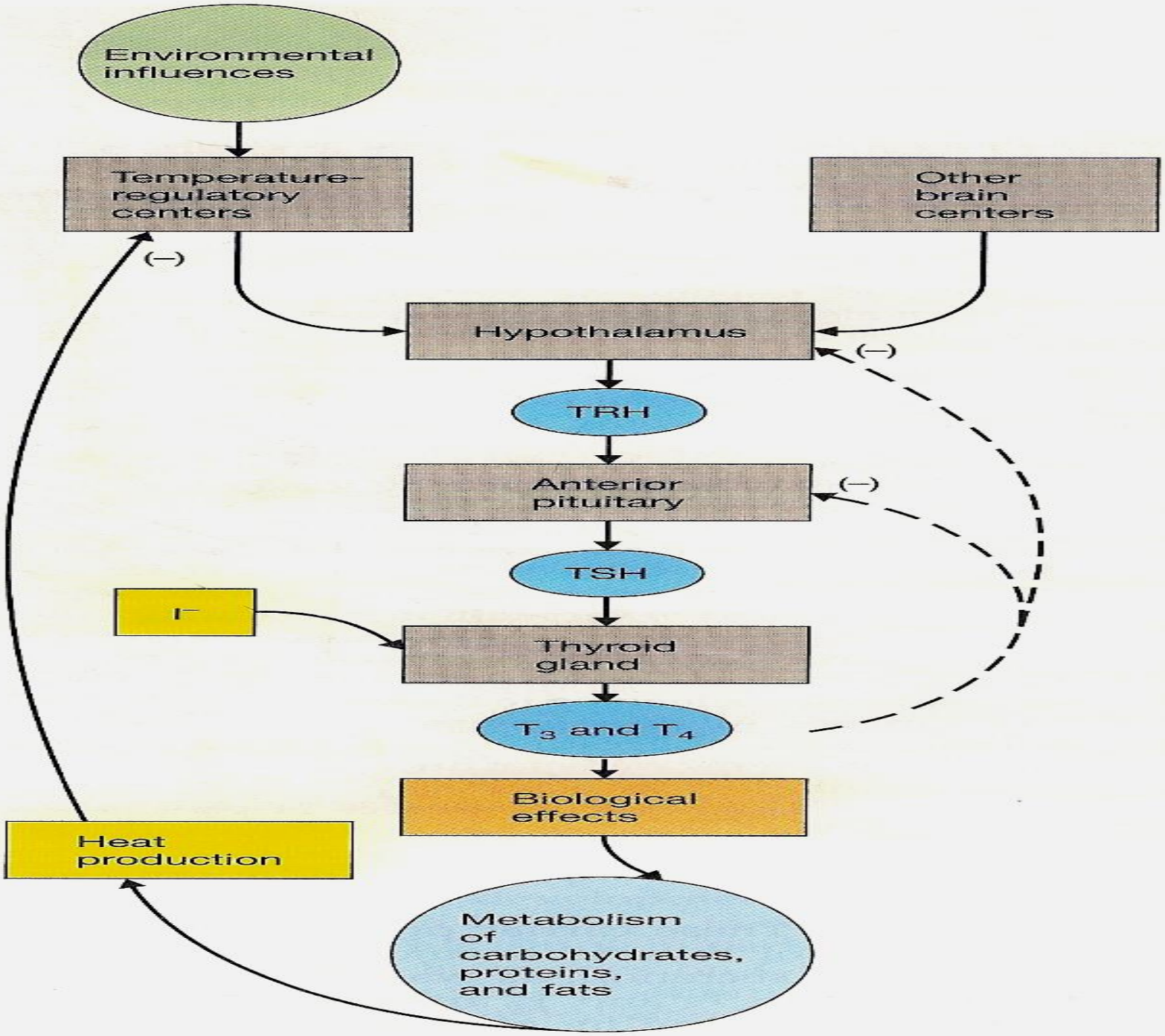
3- Enzyme 5- iodinase.

REGULATION OF HORMONES SECRETION

- It is regulated by the hypothalamic-pituitary axis.






Environmental influences
Temperature-regulatory centers
Other brain centers
(–)
Hypothalamus
(–)
TRH
Anterior pituitary
(–)
TSH
I⁻
Thyroid gland
T_3 and T_4
Biological effects
Heat production
Metabolism of carbohydrates, proteins, and fats

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	Inhibitory Factors
TSH	I^- deficiency
Thyroid-stimulating immunoglobulins	Deiodinase deficiency
Increased TBG levels (e.g., pregnancy)	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 (stat 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.
- Increase stroke volume.
- Decrease peripheral resistance.

Cardiac out put up to 60%

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