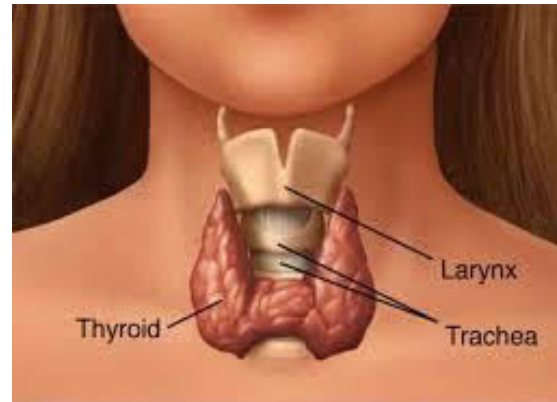


# THYROID GLAND



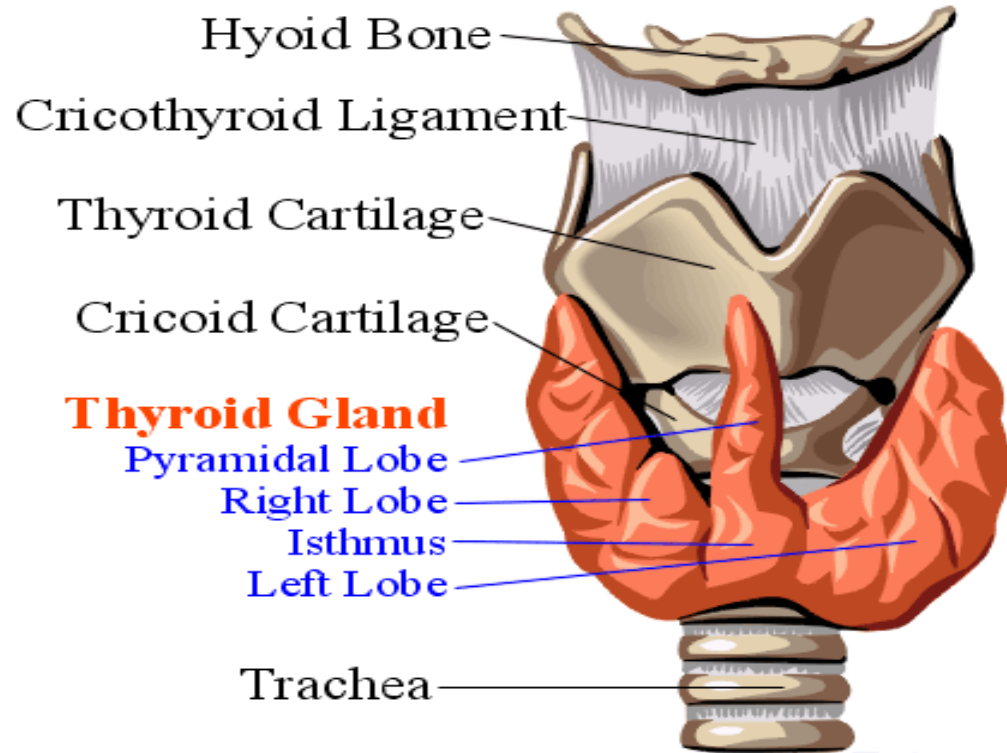
## OBJECTIVES

- **Production and secretion of thyroid hormones**
- **Transport and activities of thyroid hormones**
- **Regulation of thyroid hormone secretion**
- **Actions of thyroid hormones**
- **Hyperthyroidism and hypothyroidism**

# THE THYROID GLAND

## Functional anatomy

- Bilobed
  - Joined by isthmus
- pyramidal lobe

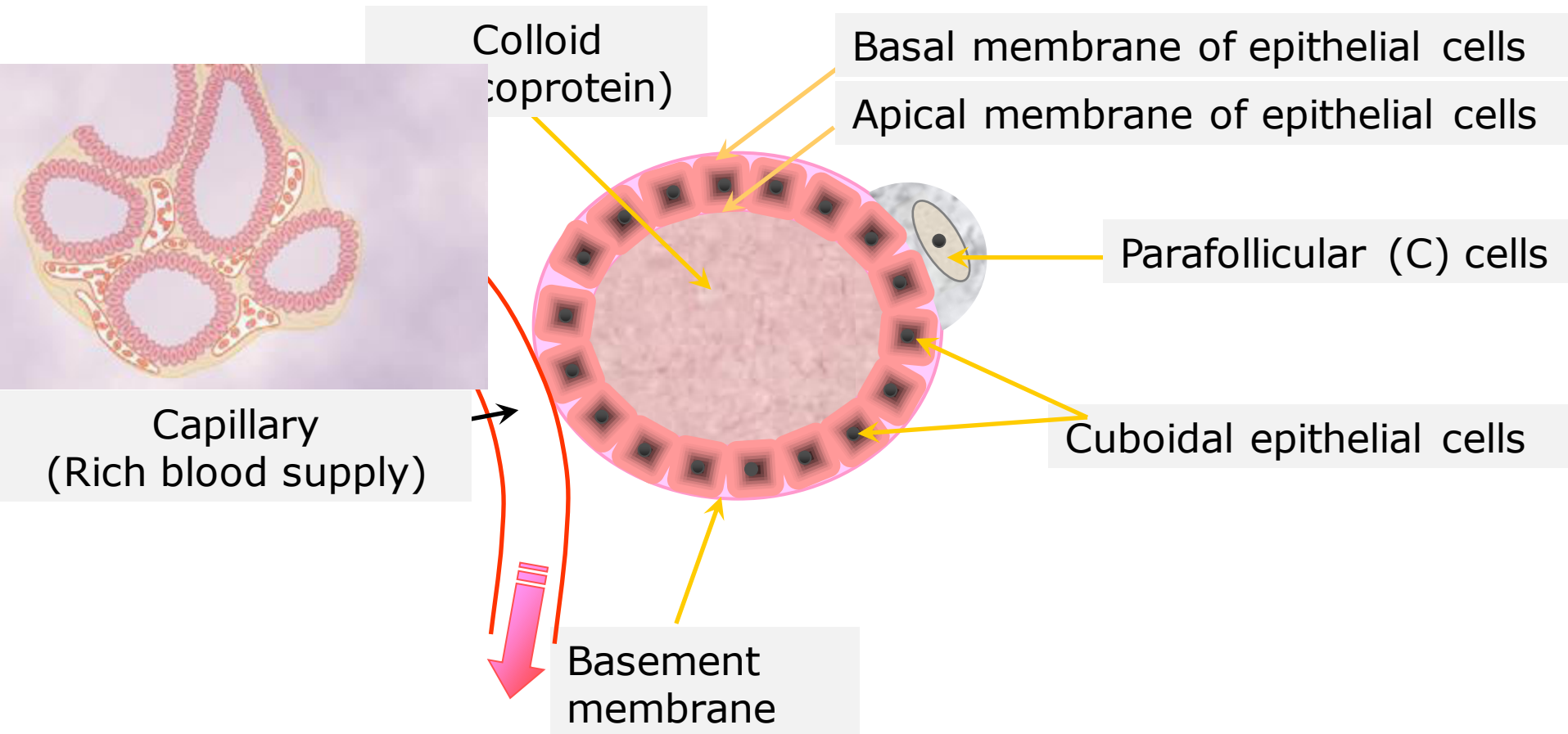


- ◎ It is the only visible endocrine gland
- ◎ It is the largest endocrine gland (15-25 gm in weight)
- ◎ Highly vascular gland
- ◎ Not essential for life
- ◎ Secretion stored extracellularly

# Structure of thyroid follicle (euthyroid gland)

● 3 Million follicles

☛ Follicle (structural and functional unit of the gland)

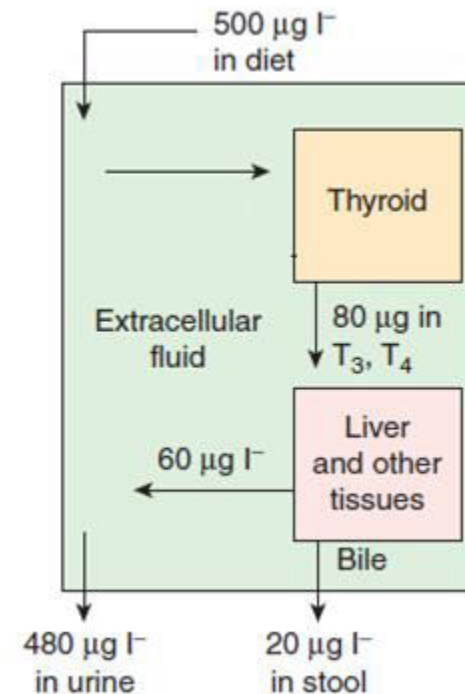


# Secretion:

- ⦿ Follicular cells → T<sub>4</sub>, T<sub>3</sub> & rT<sub>3</sub>
- ⦿ Parafollicular cells → Calcitonin

# Why is iodine important in thyroid hormone production?

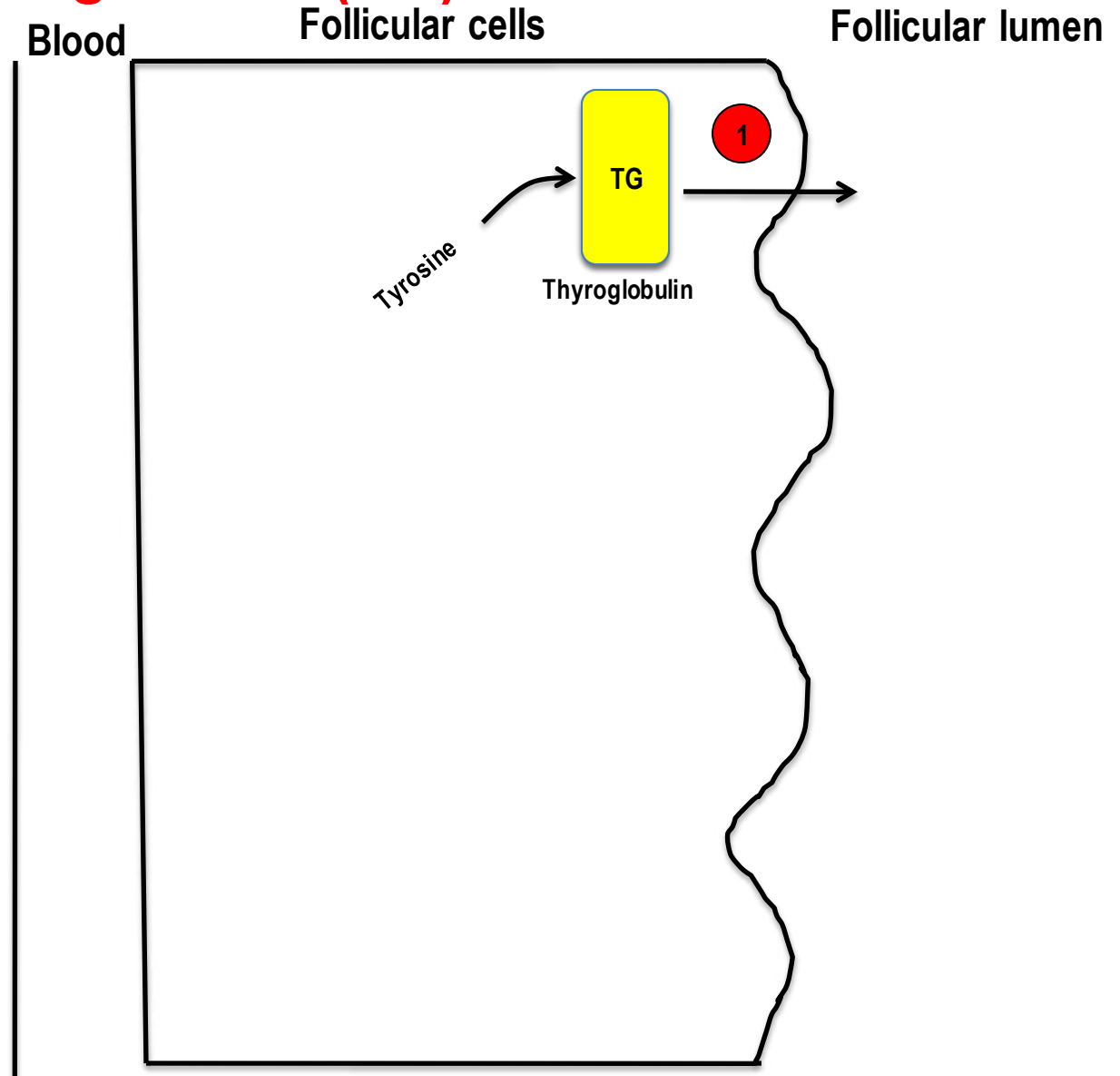
- ⦿ Thyroid hormones are unique biological molecules in that they incorporate iodine in their structure.
- ⦿ Iodine
  - ➡ Sea (plant & fish)
  - ➡ Salt 100000 NaCl/1NaI



# Synthesis and secretion of thyroid hormones

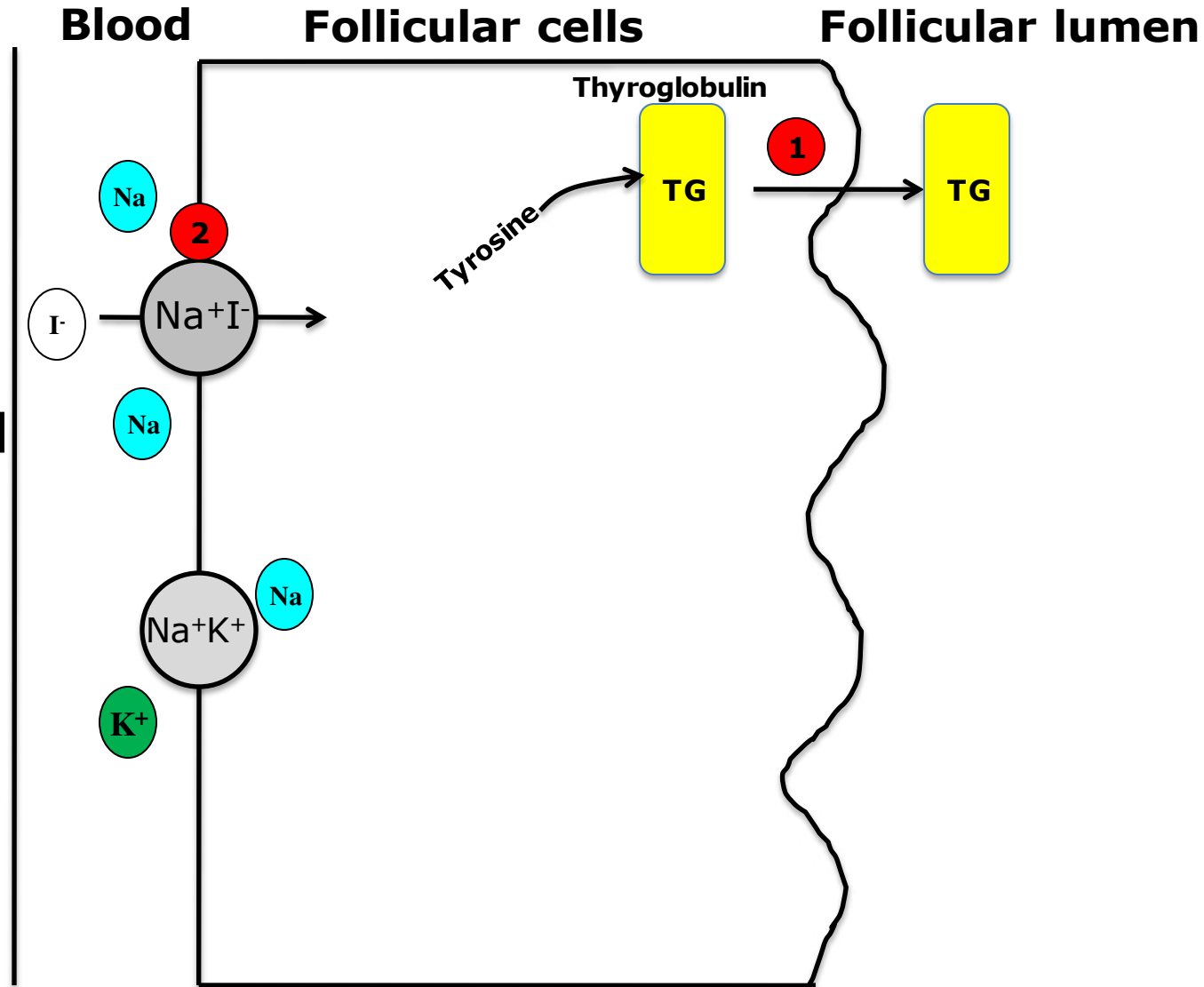
## 1. Secretion of thyroglobulin (TG)

☞ TG is synthesized from tyrosine in thyroid follicular cells, packaged in secretory vesicles, and secreted into follicular lumen



## 2. Iodide uptake (trapping)

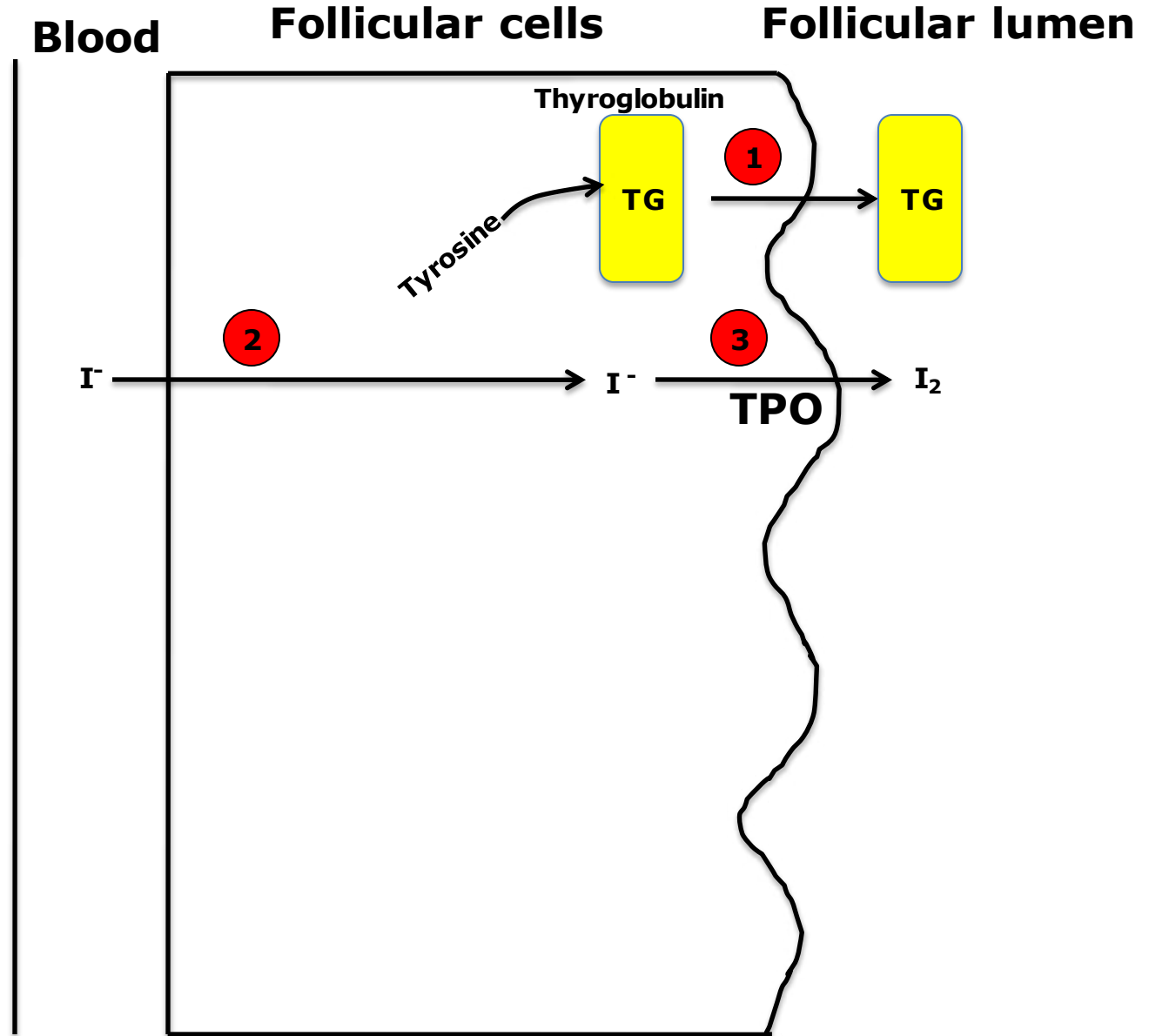
- ☞  $\text{Na}^+ \text{I}^-$  symporter
- ☞ Secondary active transport (against electrochemical gradient)
- ☞ Stimulated by TSH
- ☞ Competitively inhibited by monovalent ions (perchlorate and thiocyanate)



- Ionized iodide also taken by salivary glands, breast, gastric glands and placenta (not stimulated by TSH)

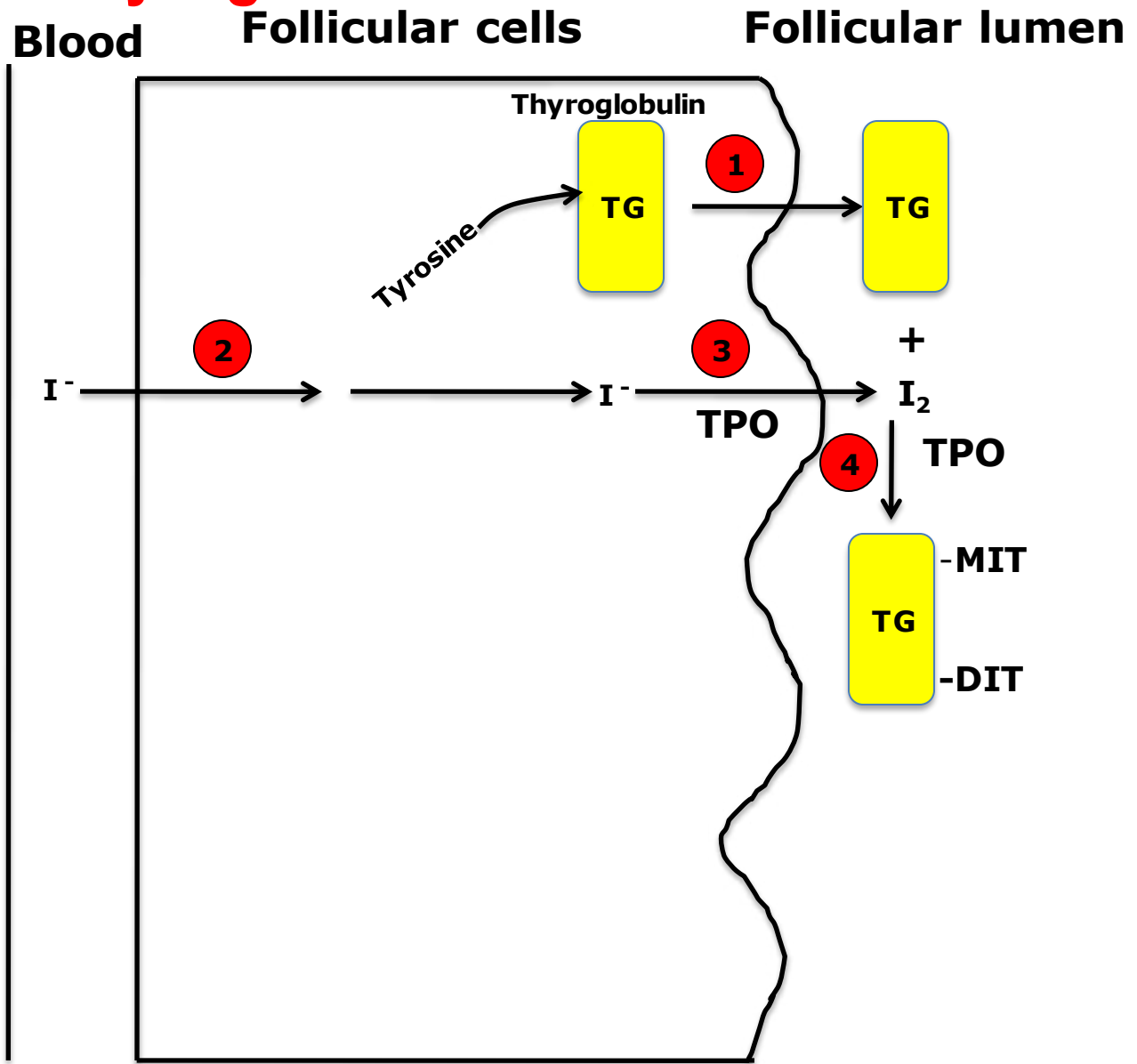
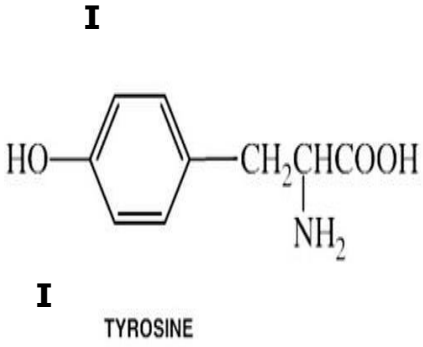
# 3. Oxidation of iodide ( $I^-$ ) to iodine ( $I_2$ )

- ☞ Thyroid peroxidase (TPO)
- ☞ In apical border of follicular cells



# 4. Organification of thyroglobulin

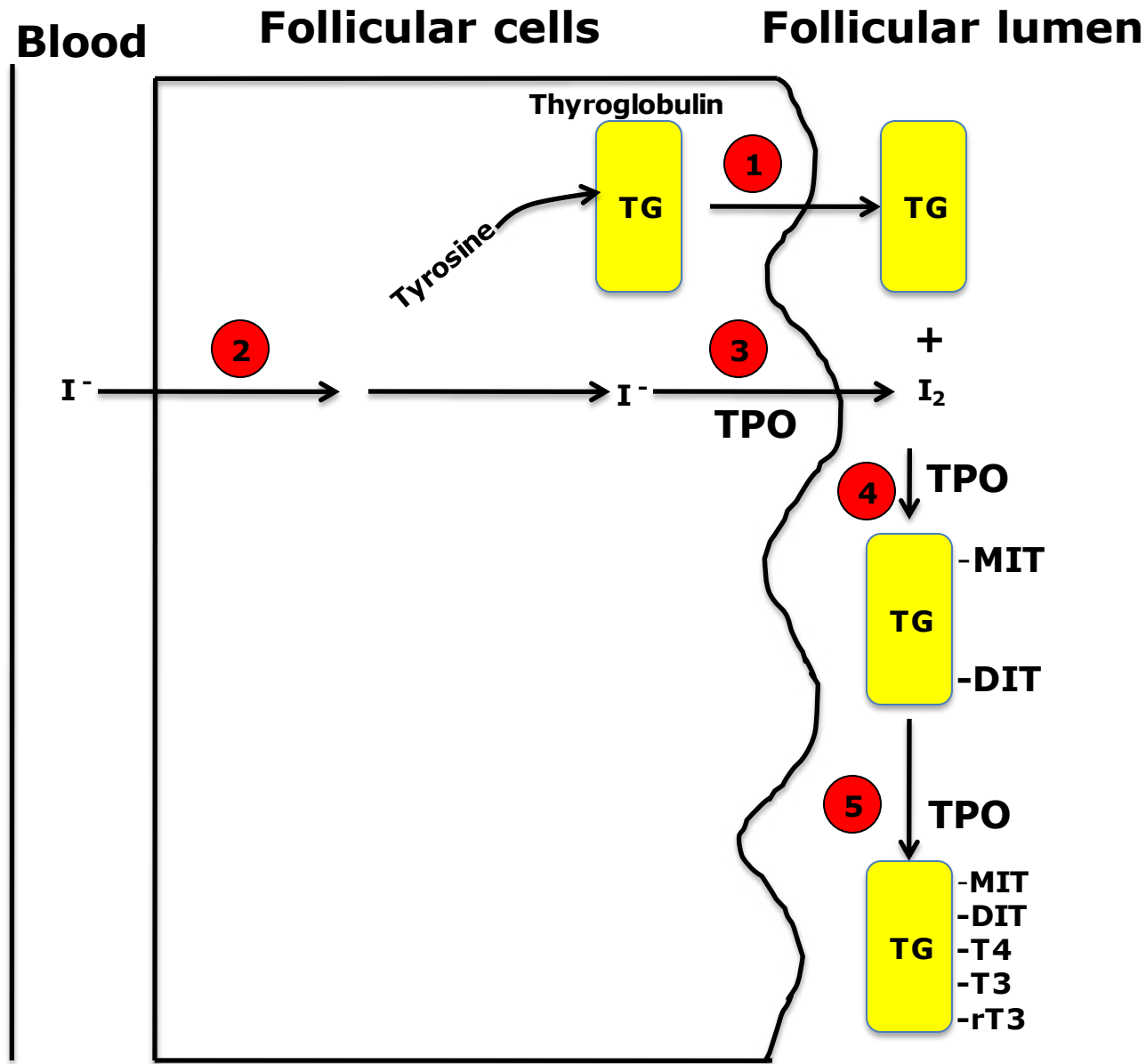
- ⬅ Iodination of tyrosine residues of thyroglobulin → MIT and DIT
- ⬅ The reaction occurs at cell-lumen interface (TPO)

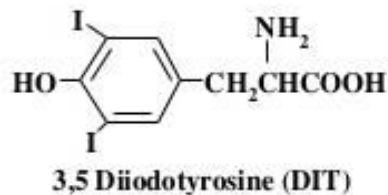




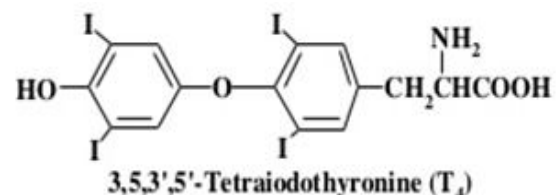
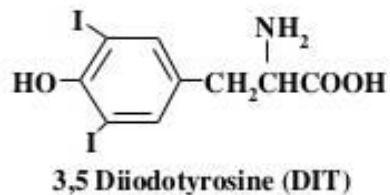
# 5. Condensation or coupling reaction

- ☞ Coupling of iodotyrosine → iodothyronine ( $T_4$ ,  $T_3$  &  $rT_3$ )
- ☞ TPO
- ☞ TPO inhibited by antithyroid drugs
  - Propylthiouracil
  - Carbimazole
  - Methimazole

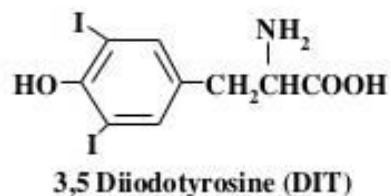
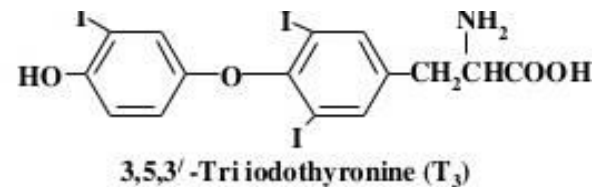
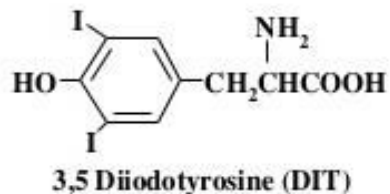




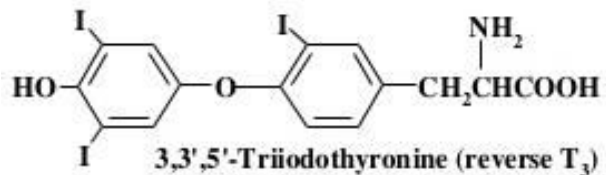
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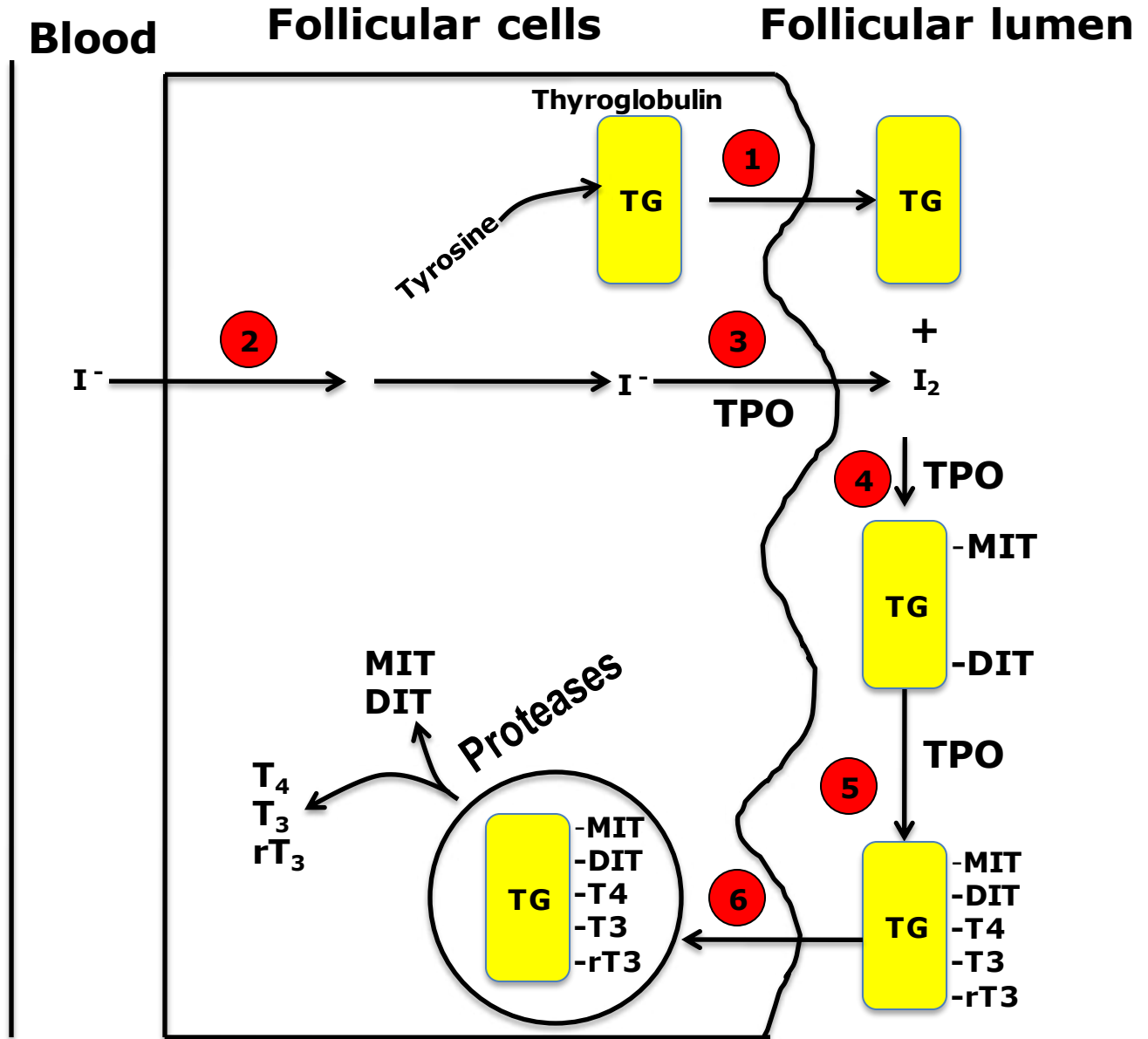


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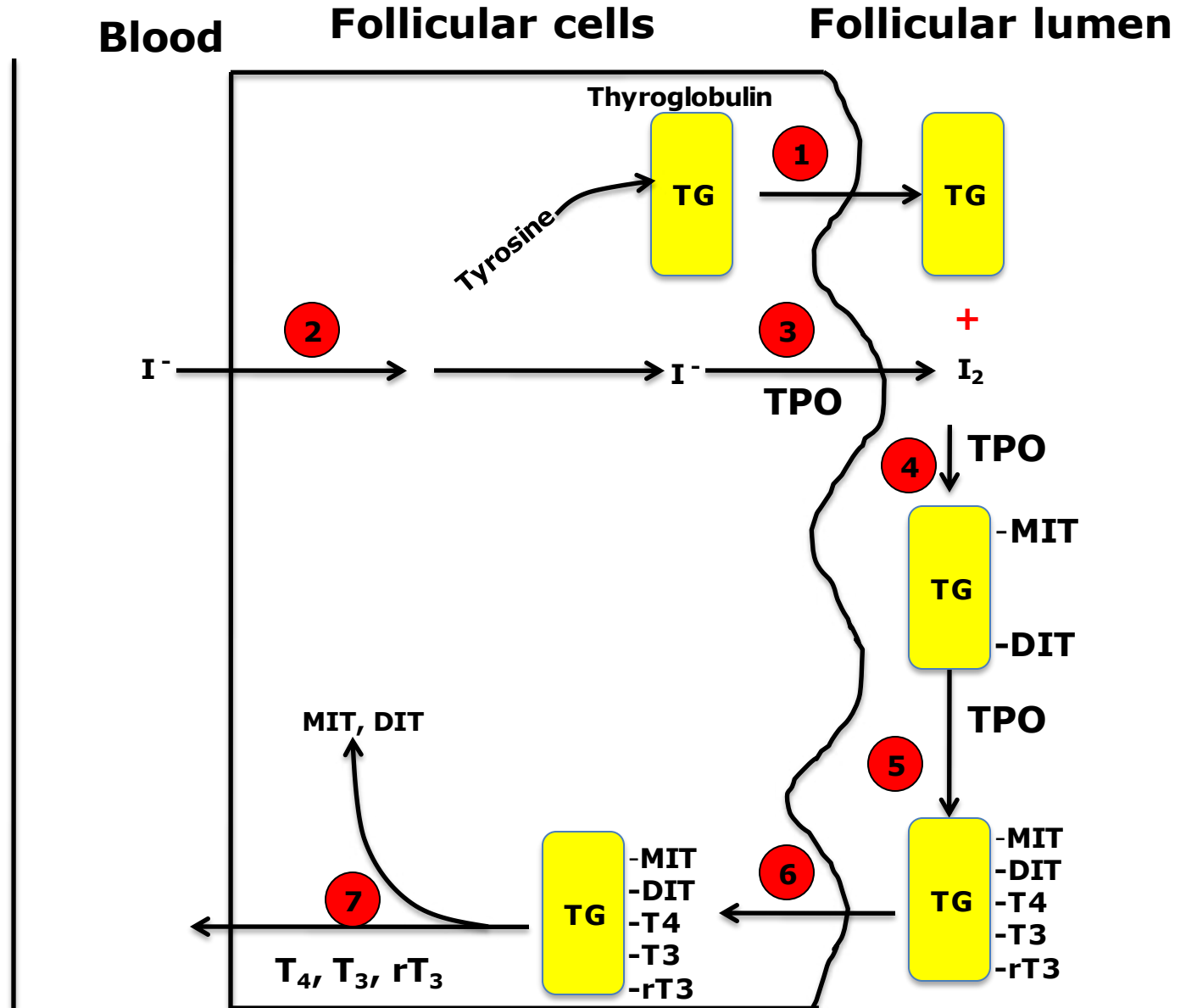


# 6. Pinocytosis

- ☞ Pinocytic vesicles
- ☞ Proteases → release of iodinated compounds



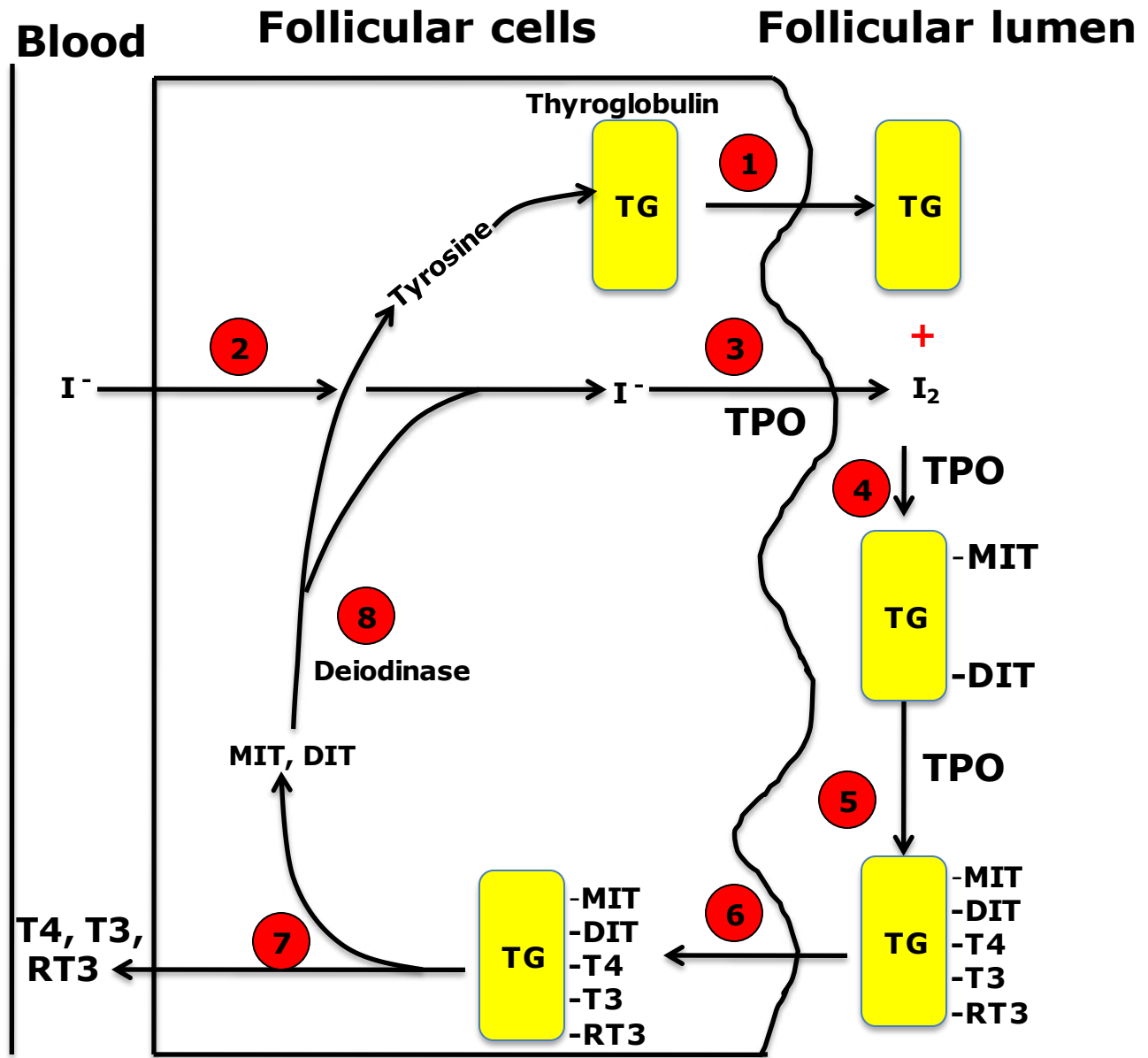
# 7. Secretion of $T_4$ , $T_3$ , and $rT_3$



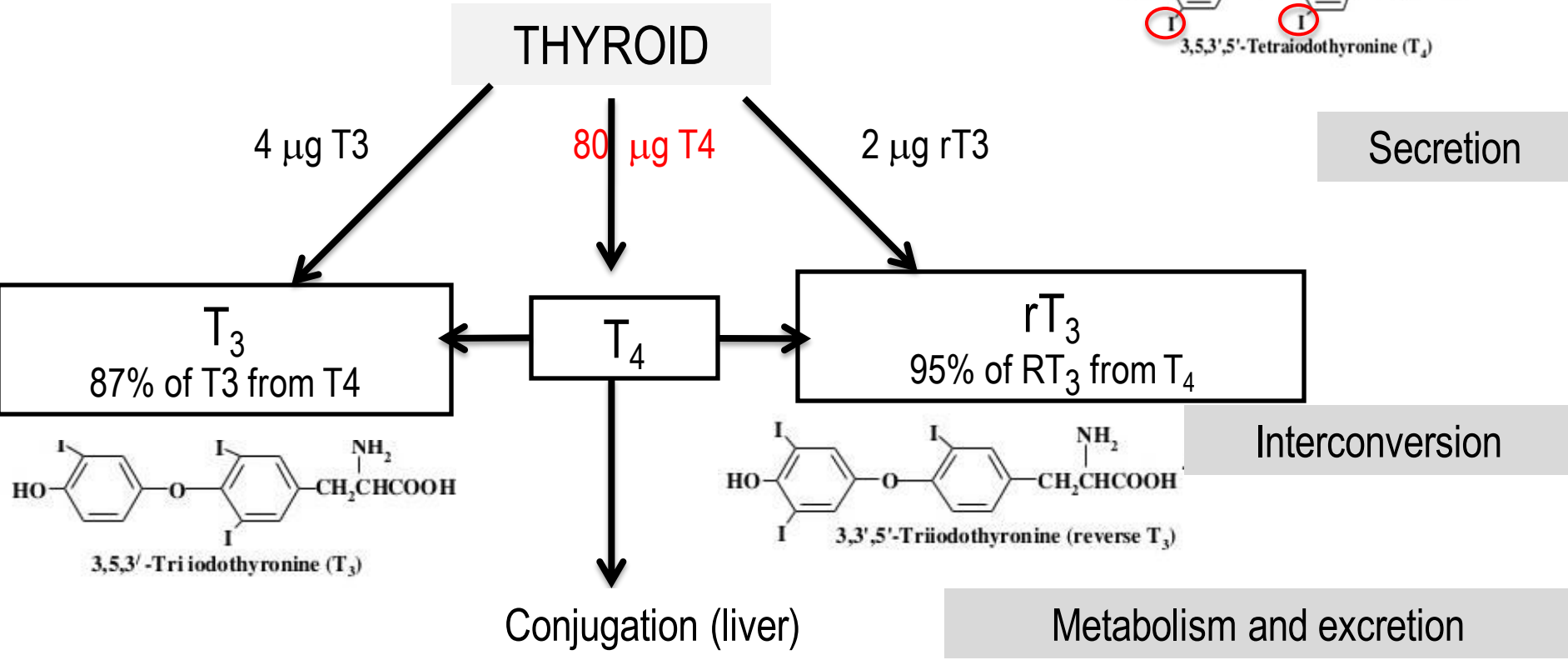
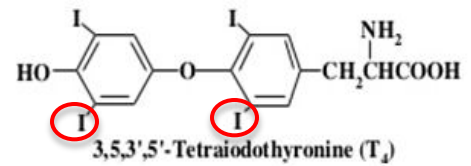
# 8. Deiodination of MIT and DIT

☞ Deiodinase enzyme

All steps of thyroid hormone synthesis and secretion are stimulated by TSH



# Metabolism of thyroid hormones



<b>T3 4 times more active than T4</b>	<b>T3</b>	<b>T4</b>
Free	More	less
Binding to nuclear receptors	More	less
Activity	Potent rapid	less
	½ life 1 day	7 days

# Transport of thyroid hormones

> 99% bound to plasma protein

- Thyroxine binding globulin (TBG) 70%
- Albumin
- Prealbumin (thyroxine binding prealbumin-TBPA)

**TBG ↓ in liver and kidney diseases**

**↓ Total**

**Free normal**

↓ TBG → ↓ Bound → ↑ Free → ↓ TSH → ↓ Secretion → ↓ Total (free normal)

**TBG ↑ Estrogen**

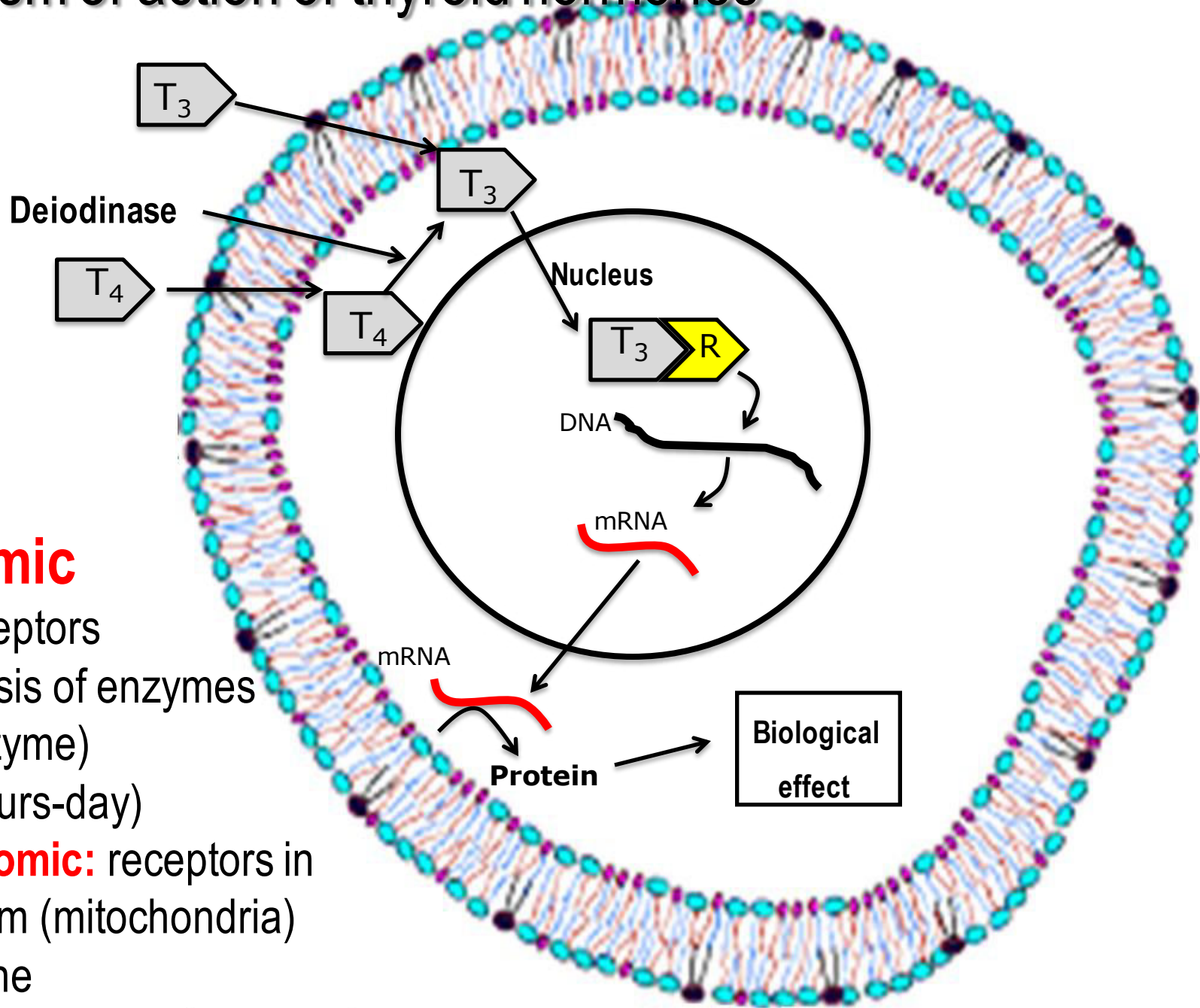
**Pregnancy, contraceptive pills**

**↑ Total**

**Free normal**

↑ TBG → ↑ Bound → ↓ Free → ↑ TSH → ↑ Secretion → ↑ Total (free normal)

# Mechanism of action of thyroid hormones



## 1) Genomic

Nuclear receptors

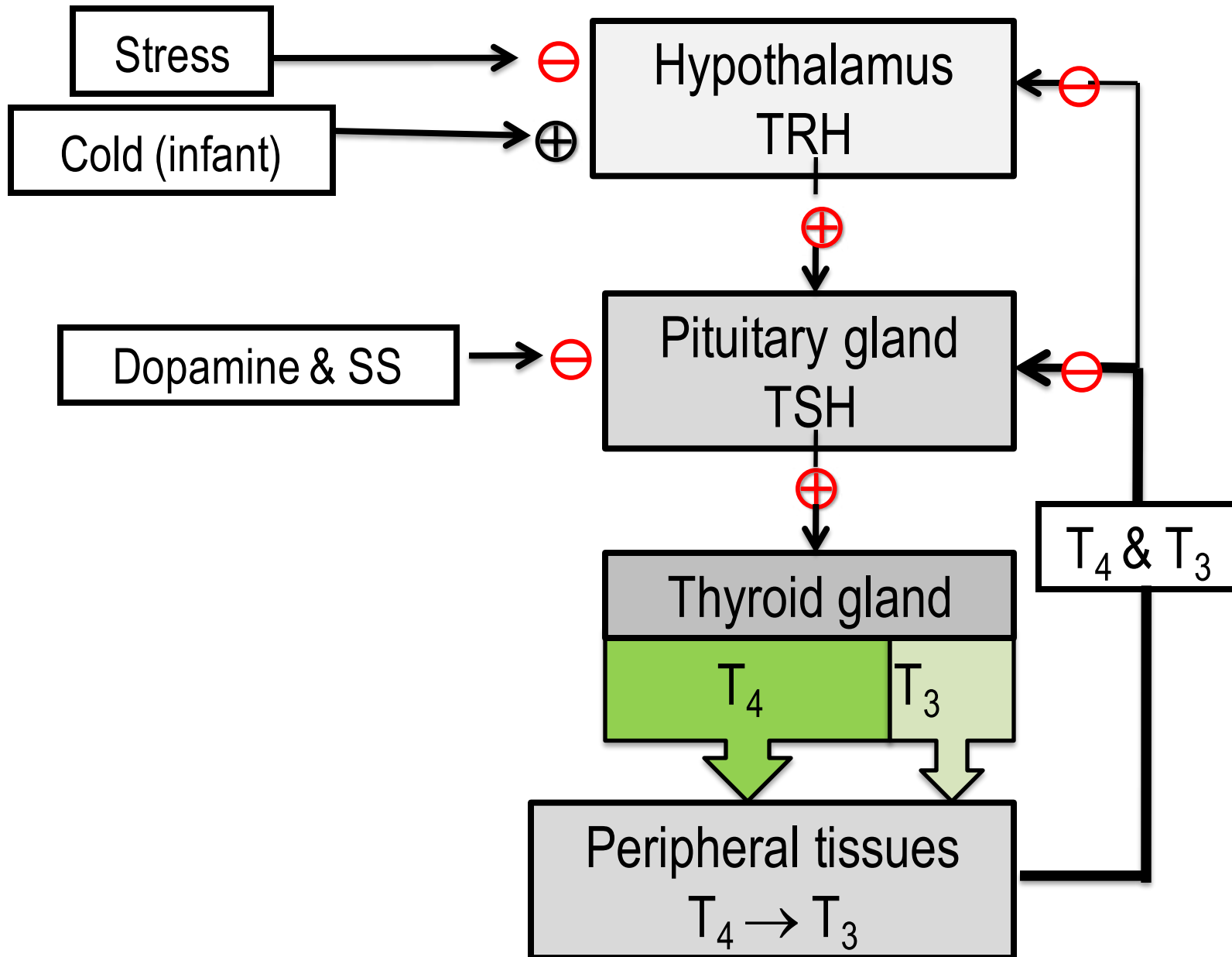
- ↑Synthesis of enzymes (250 enzyme)
- Slow (hours-day)

## 2) Non genomic: receptors in

- Cytoplasm (mitochondria)
- Membrane



# Regulation of thyroid hormone secretion



# Effects of TSH (Thyrotropin) on thyroid gland

## Glycoprotein act via cAMP

⊙ Immediate (30 min) → ↑ release of hormones  
⇒ ↑ Endocytosis and proteolysis of thyroglobulin

⊙ Slow (hours, days, weeks)

⇒ ↑ Synthesis

- ↑ Iodide trapping
- ↑ Iodination
- ↑ Coupling

⇒ Structure

- Hyperplasia and hypertrophy of follicular cells
- ↑ Blood flow

