

THE THYROID GLAND

DR. ABDULMAJEED AL-DREES

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.**

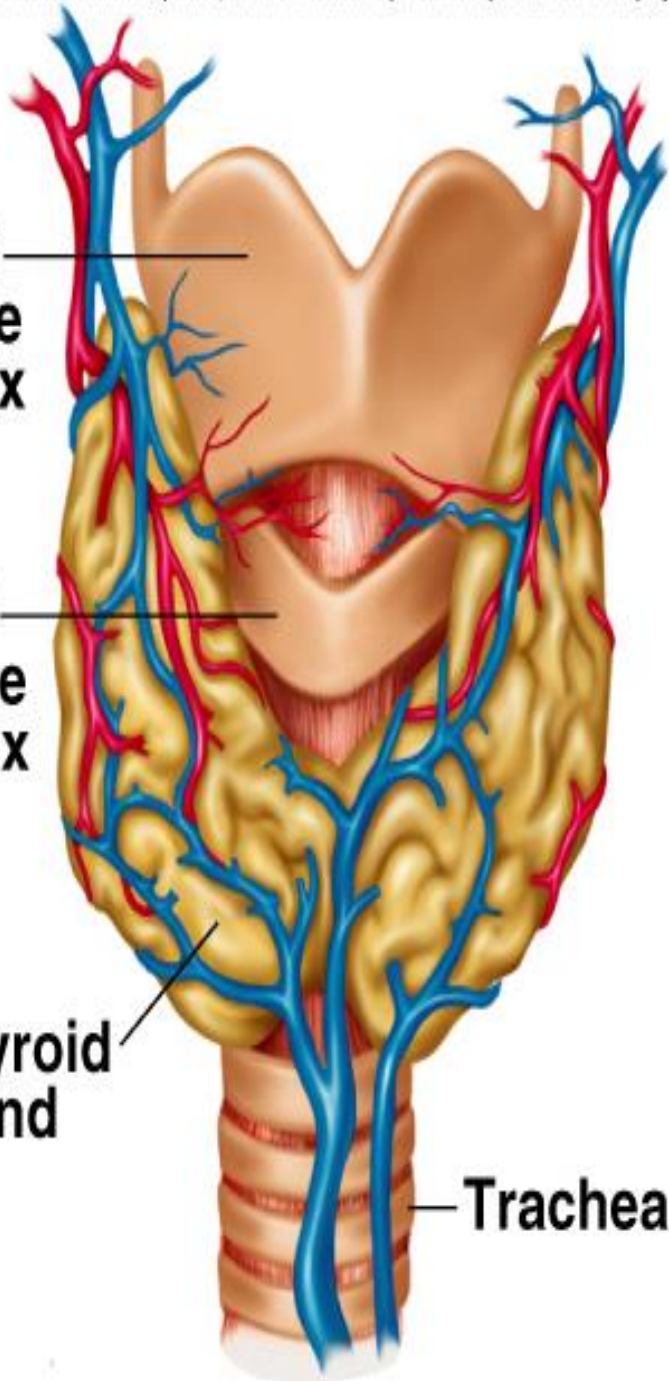
Thyroid cartilage of larynx

Cricoid cartilage of larynx

Thyroid gland

Trachea

(a)



R. external carotid A.

R. superior thyroid A.

Veins to internal R. jugular V.

R. inferior thyroid A.

Inferior thyroid Vs.

R. subclavian A.

Thyroid cartilage

Left lobe of thyroid gland

Isthmus of thyroid gland

Trachea

L. common carotid A. (cut)

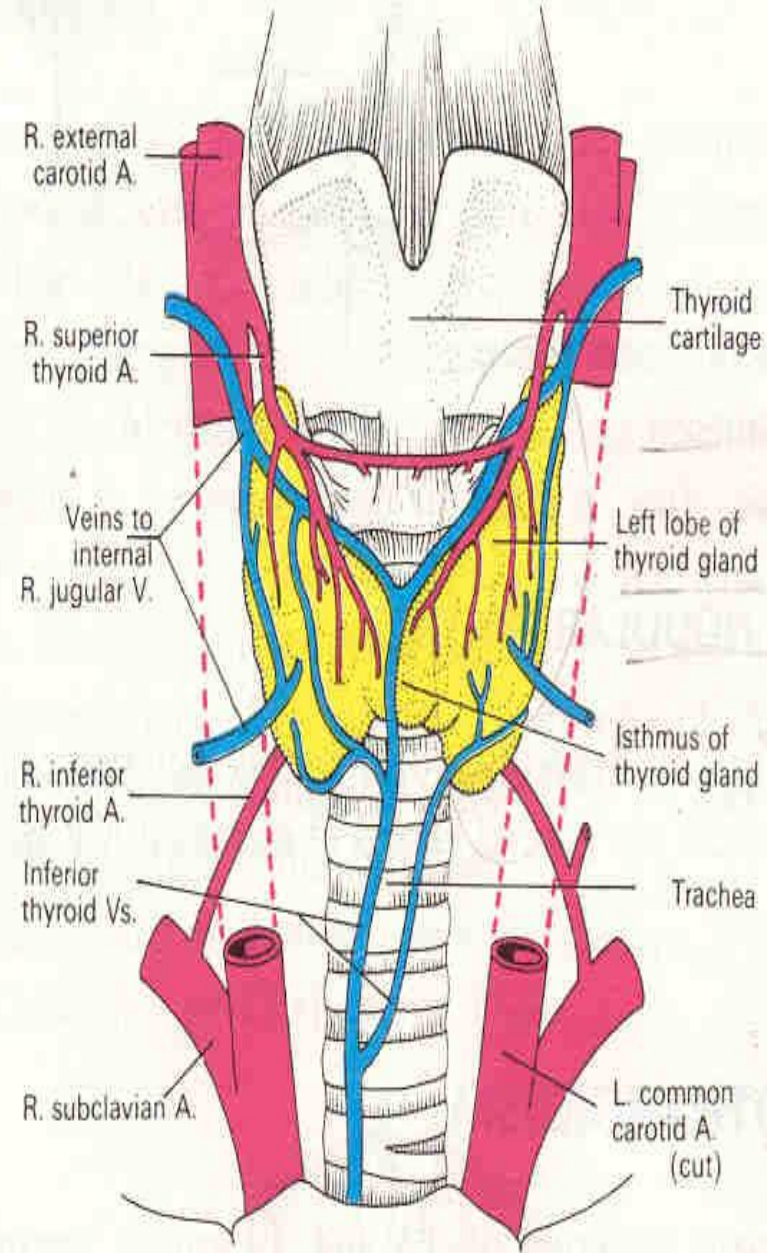
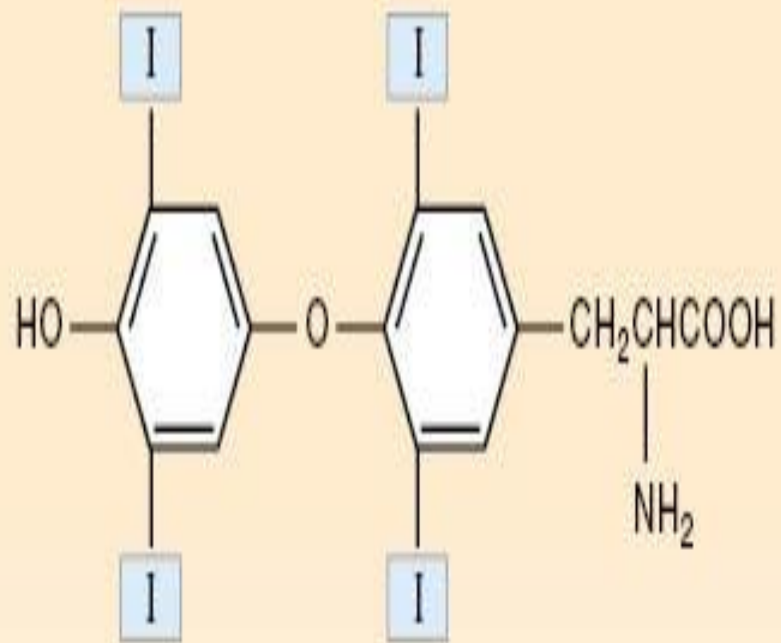


Figure 14:8 Position of thyroid gland and associated structures.

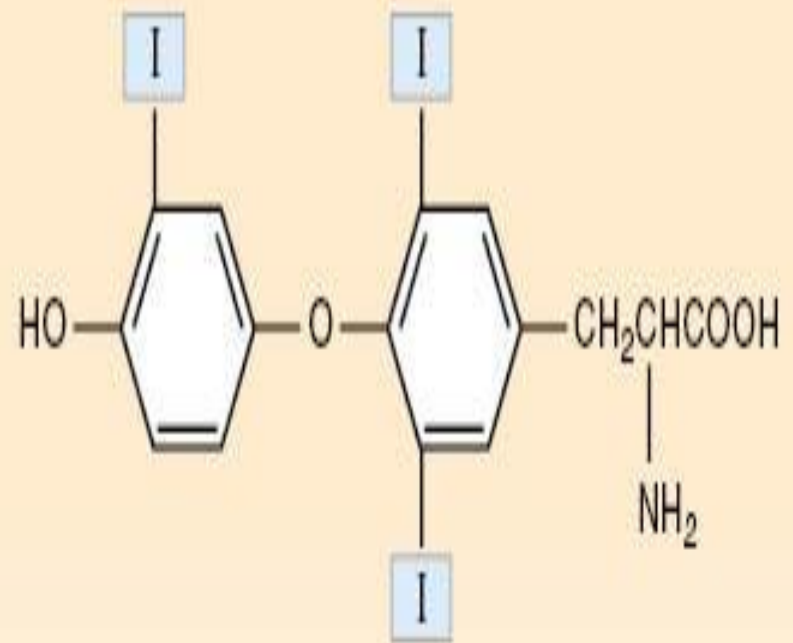
HORMONES

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

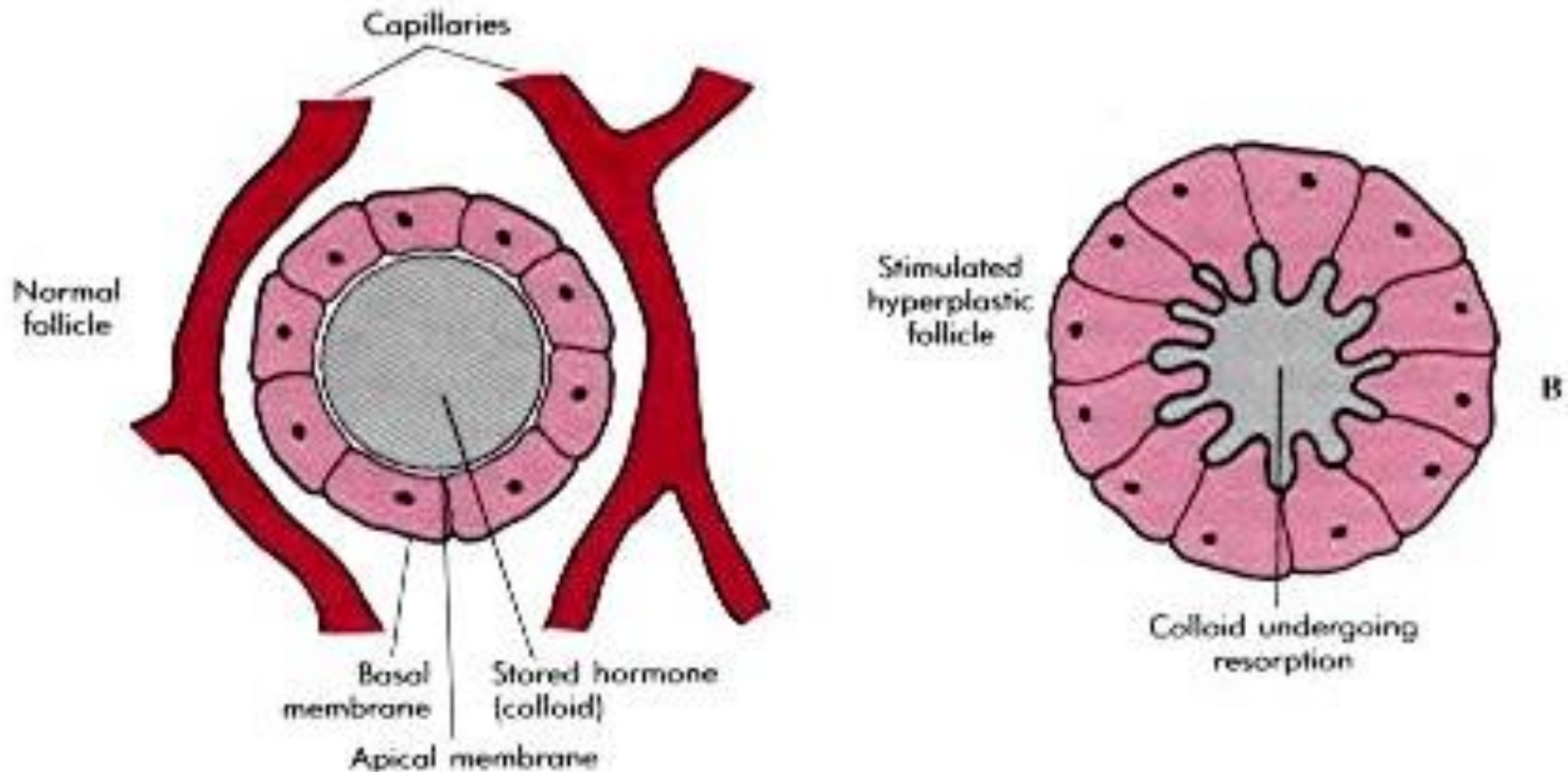
Thyroxine (T_4)



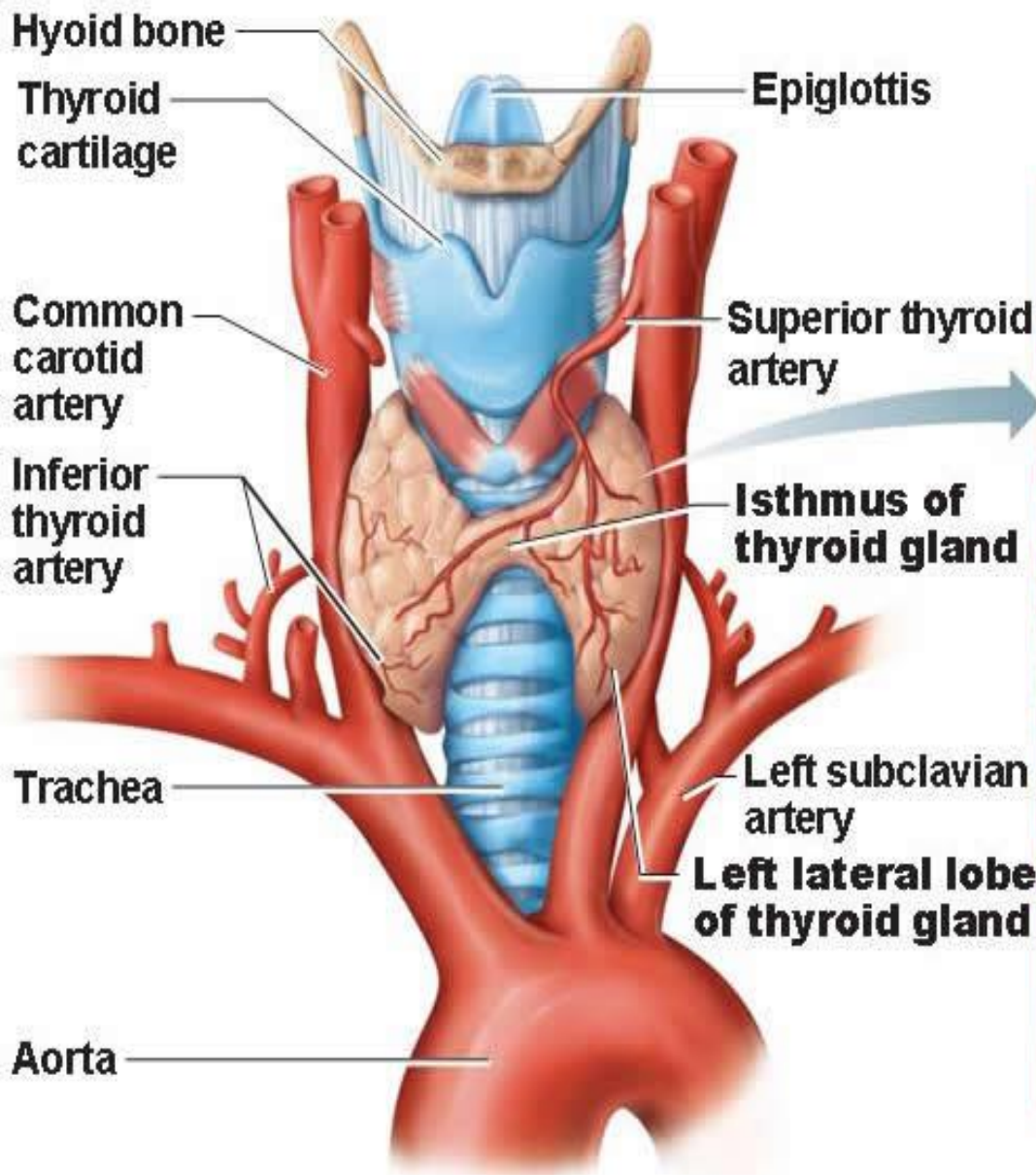
Triiodothyronine (T_3)



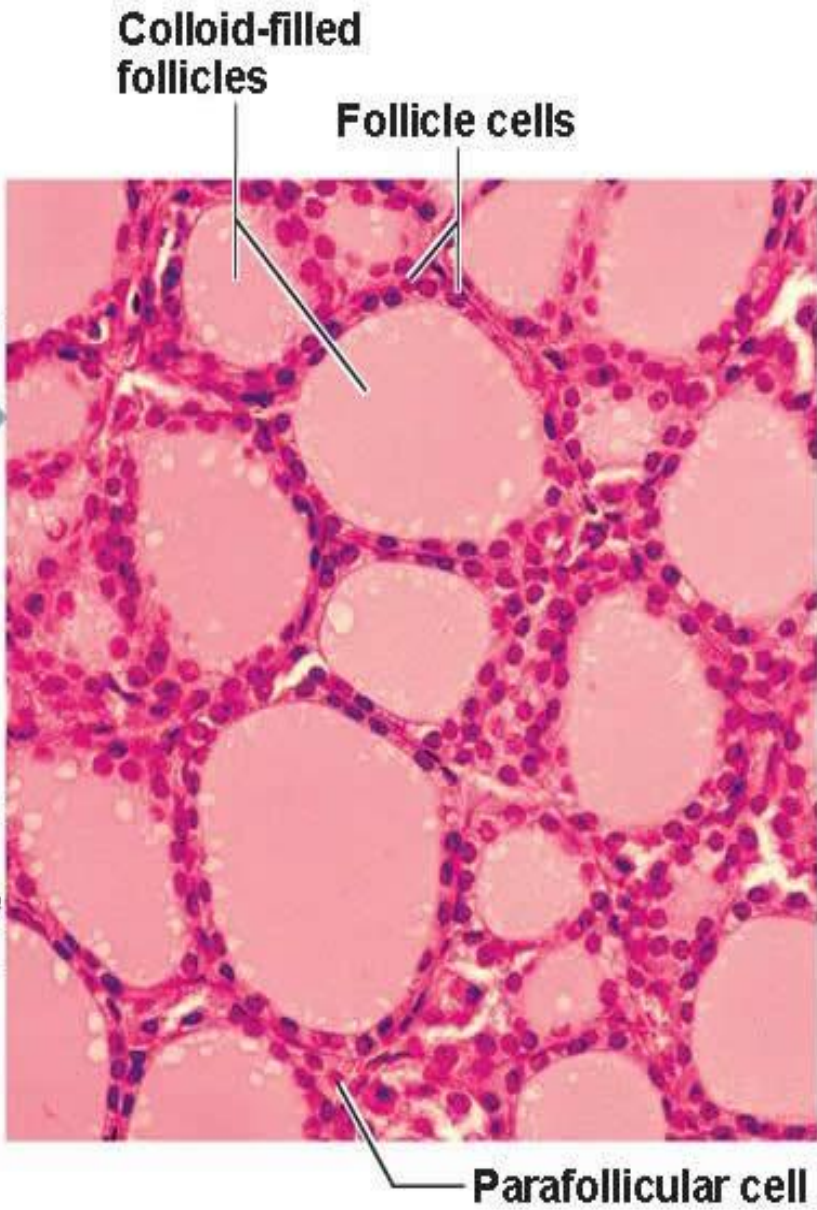
SYNTHESIS



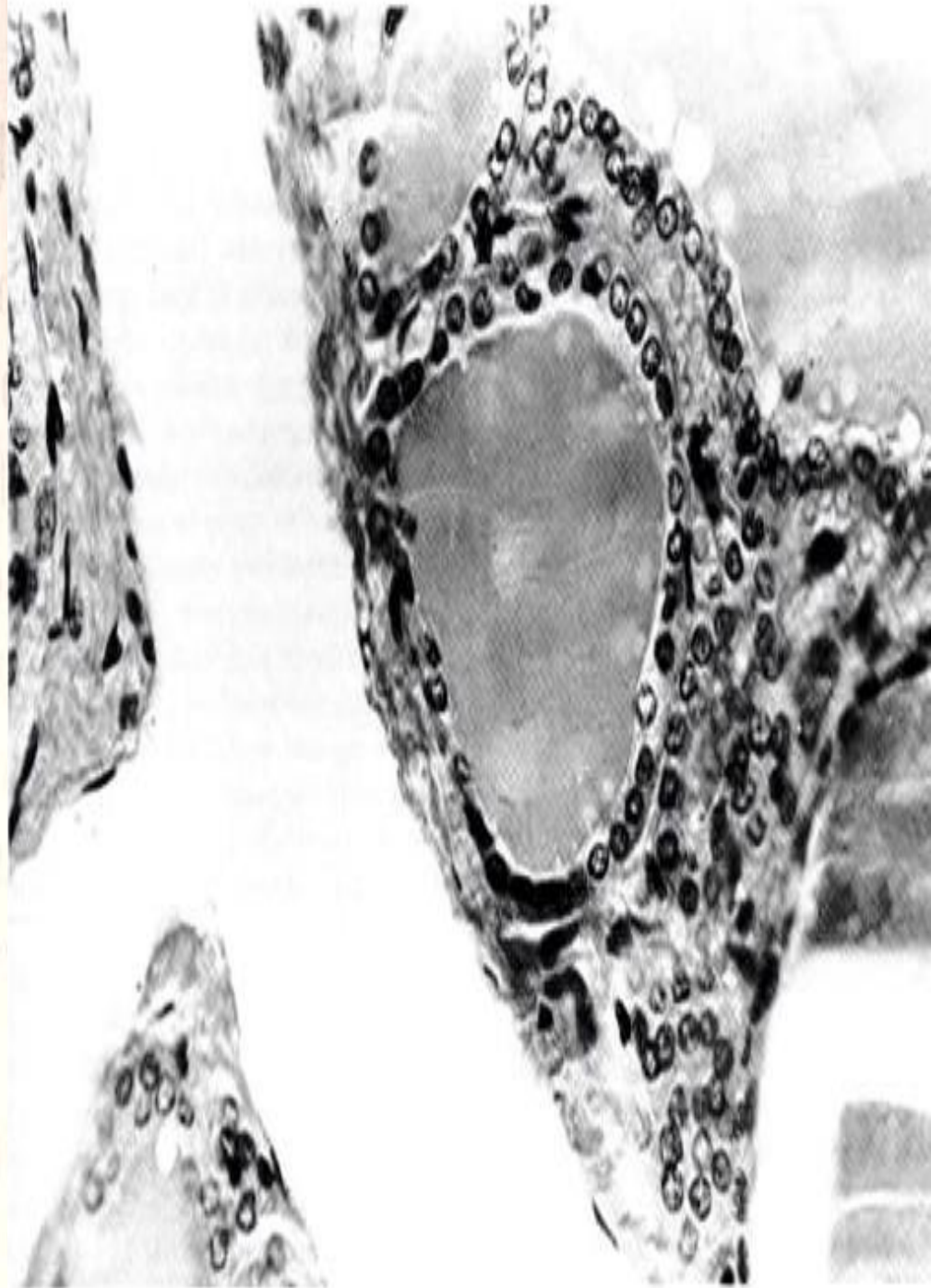
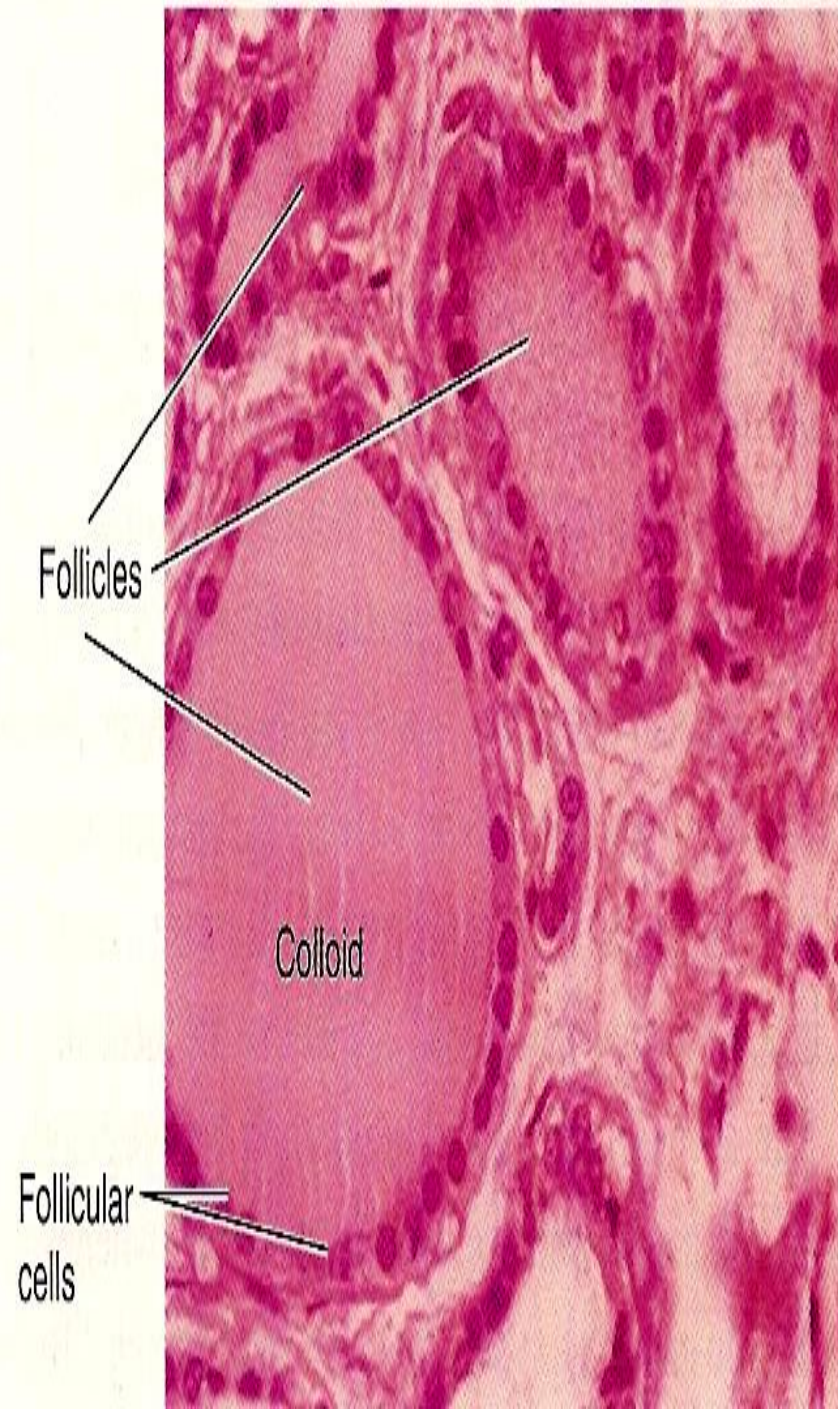
■ Fig. 49-1 A, Photomicrograph of thyroid gland follicle. B, Schematic drawing of normal thyroid gland follicle and a follicle stimulated by thyrotropin. Note change in shapes from cuboidal to columnar, relocation of nuclei to base of cells, and scalloped appearance of follicle lumen.



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



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

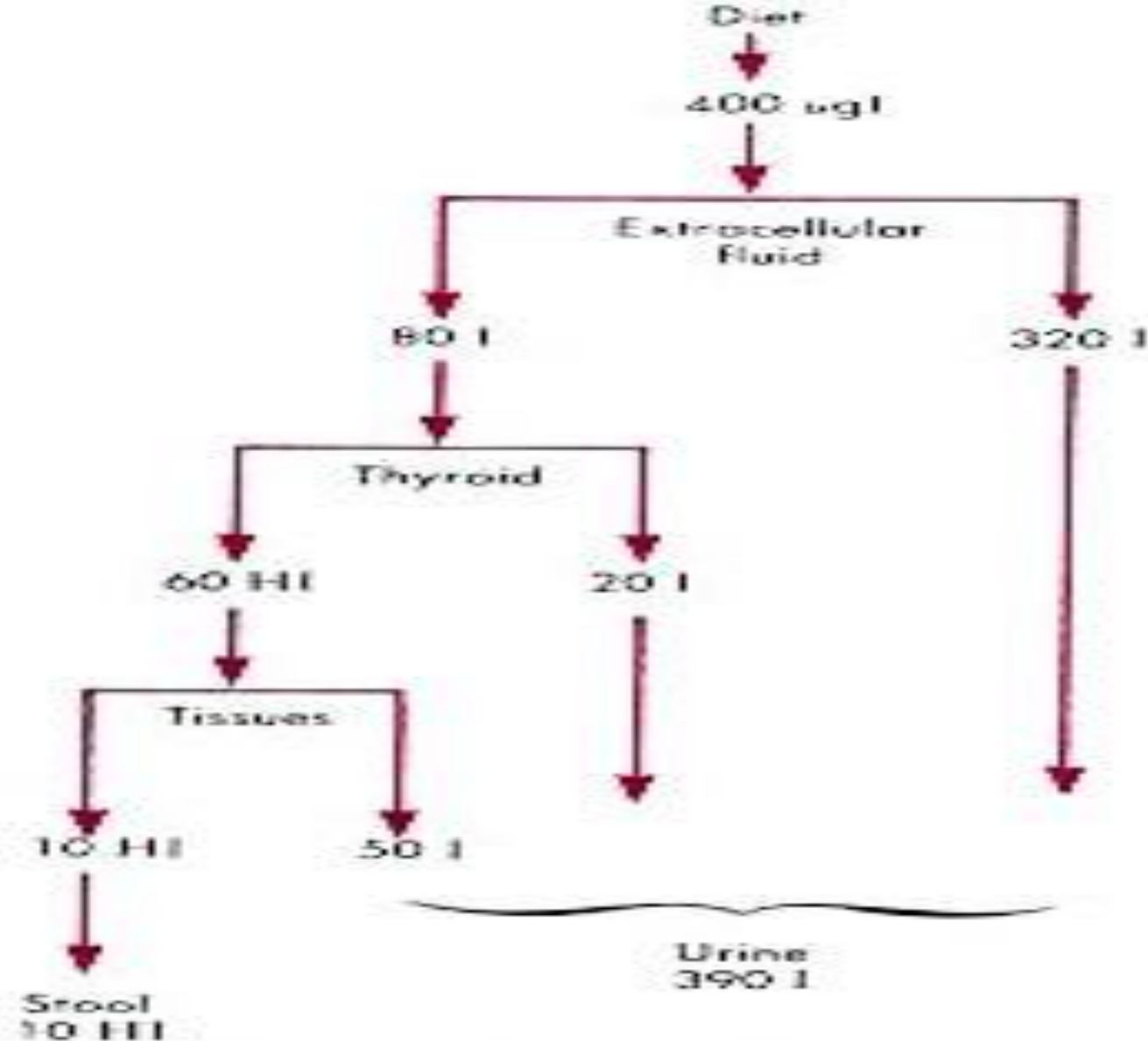


THREE UNIQUE FEATURES

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.**

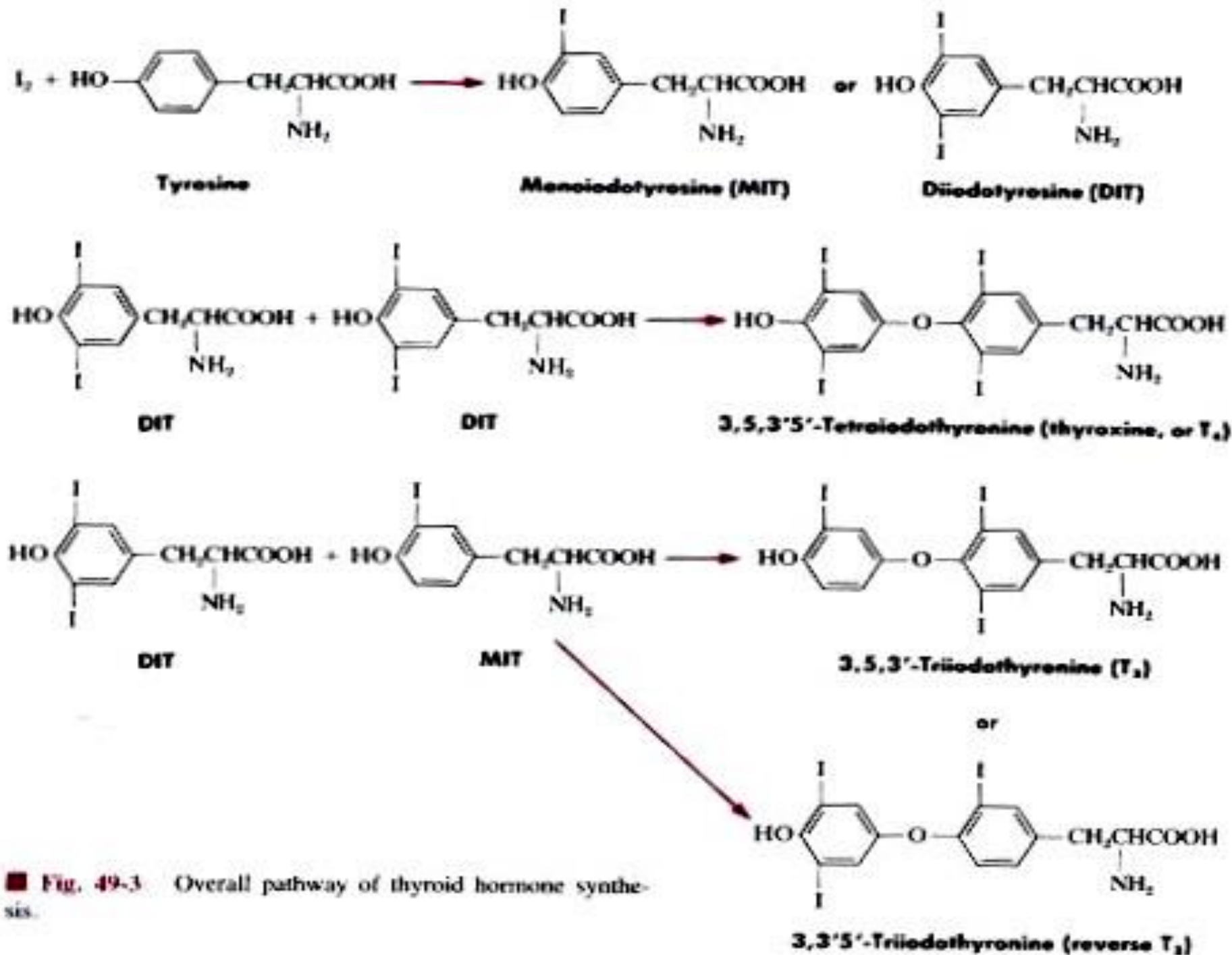
4- ORGANIFICATION OF THYROGLOBULIN

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

5- COUPLING REACTION:



- 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.

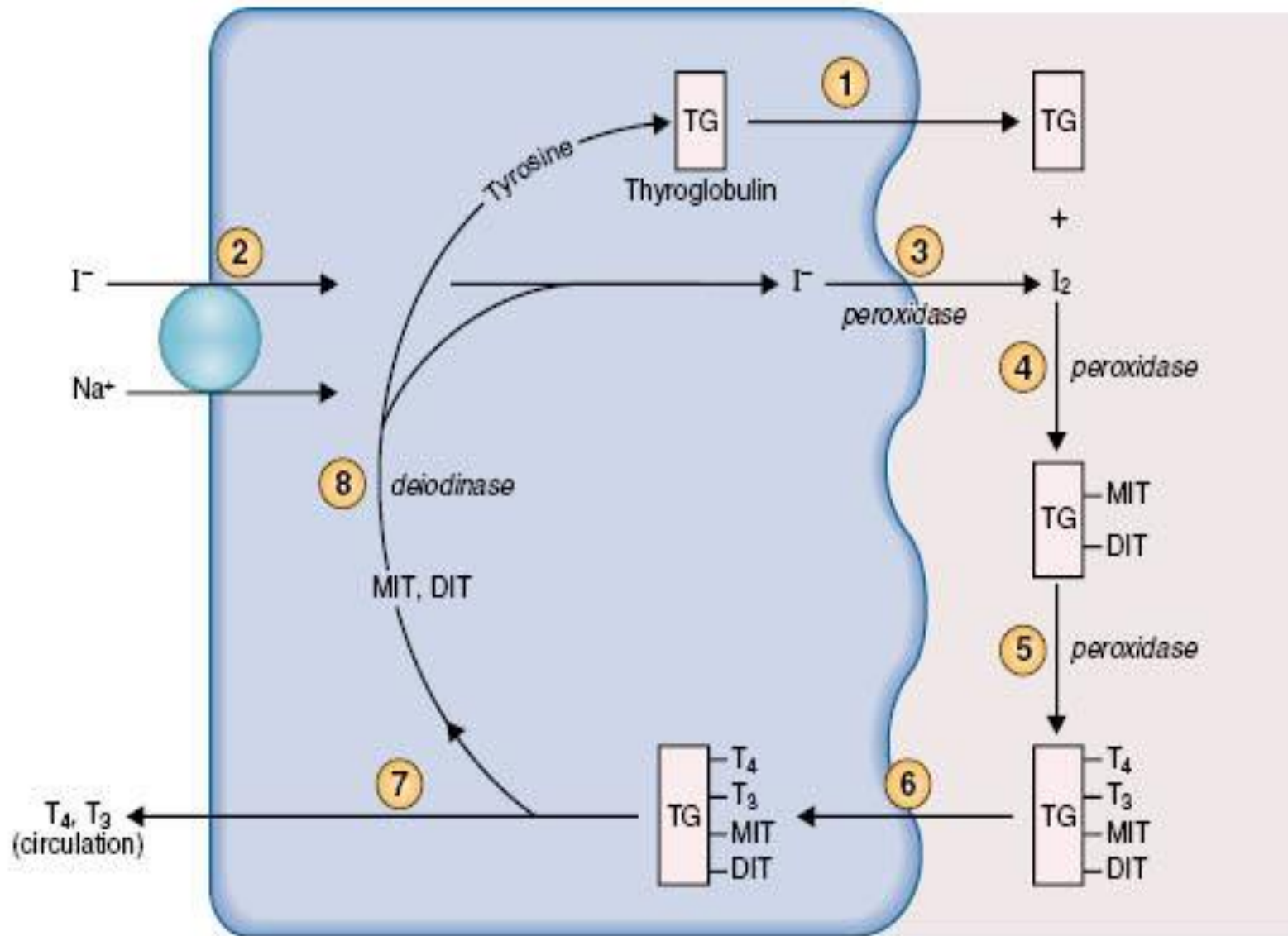
9- Delivery of T₄ and T₃ to the systemic circulation.

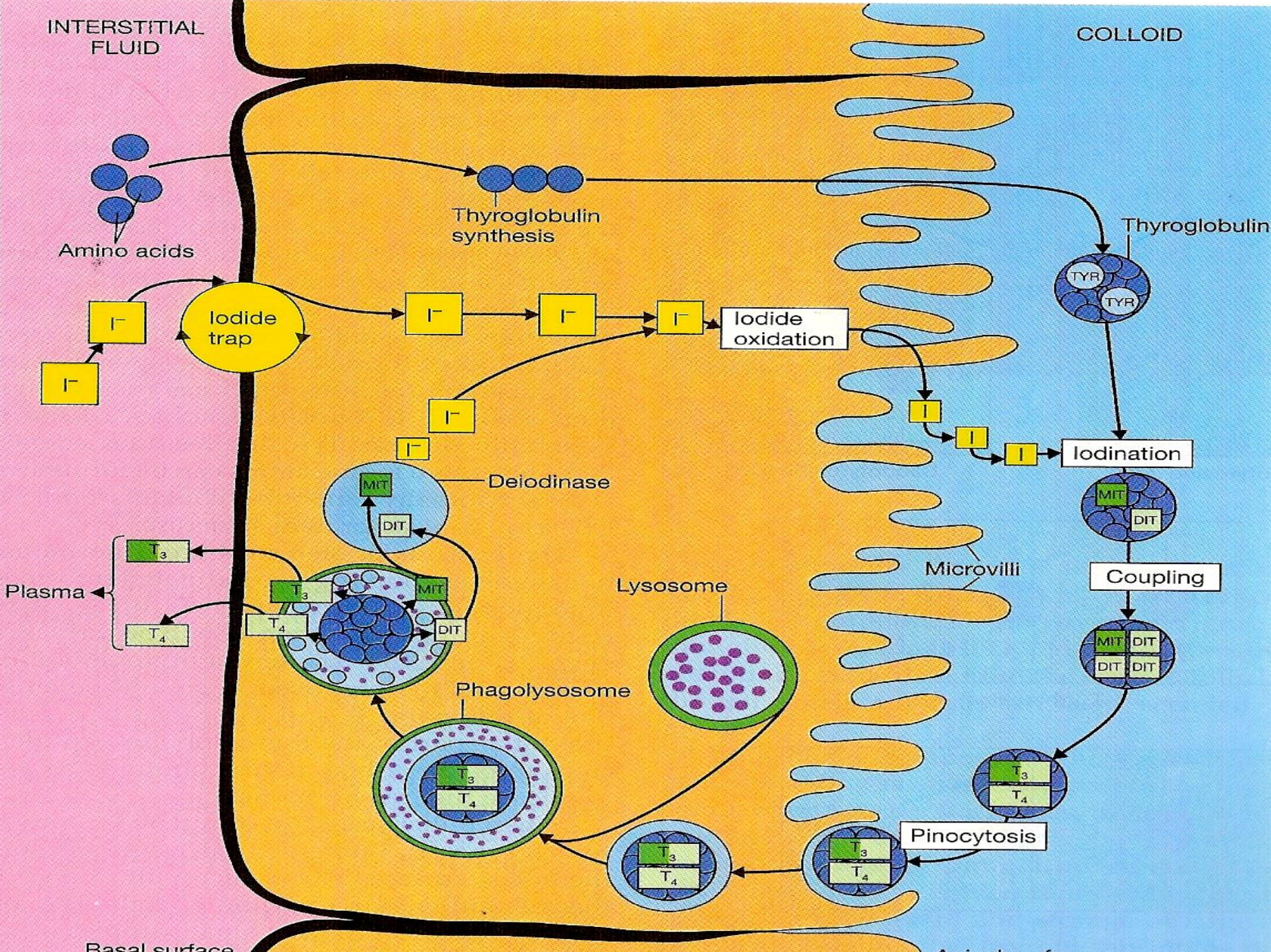
10- Deiodination of DIT and MIT by thyroid deiodinase.

Blood

Follicular epithelial cell

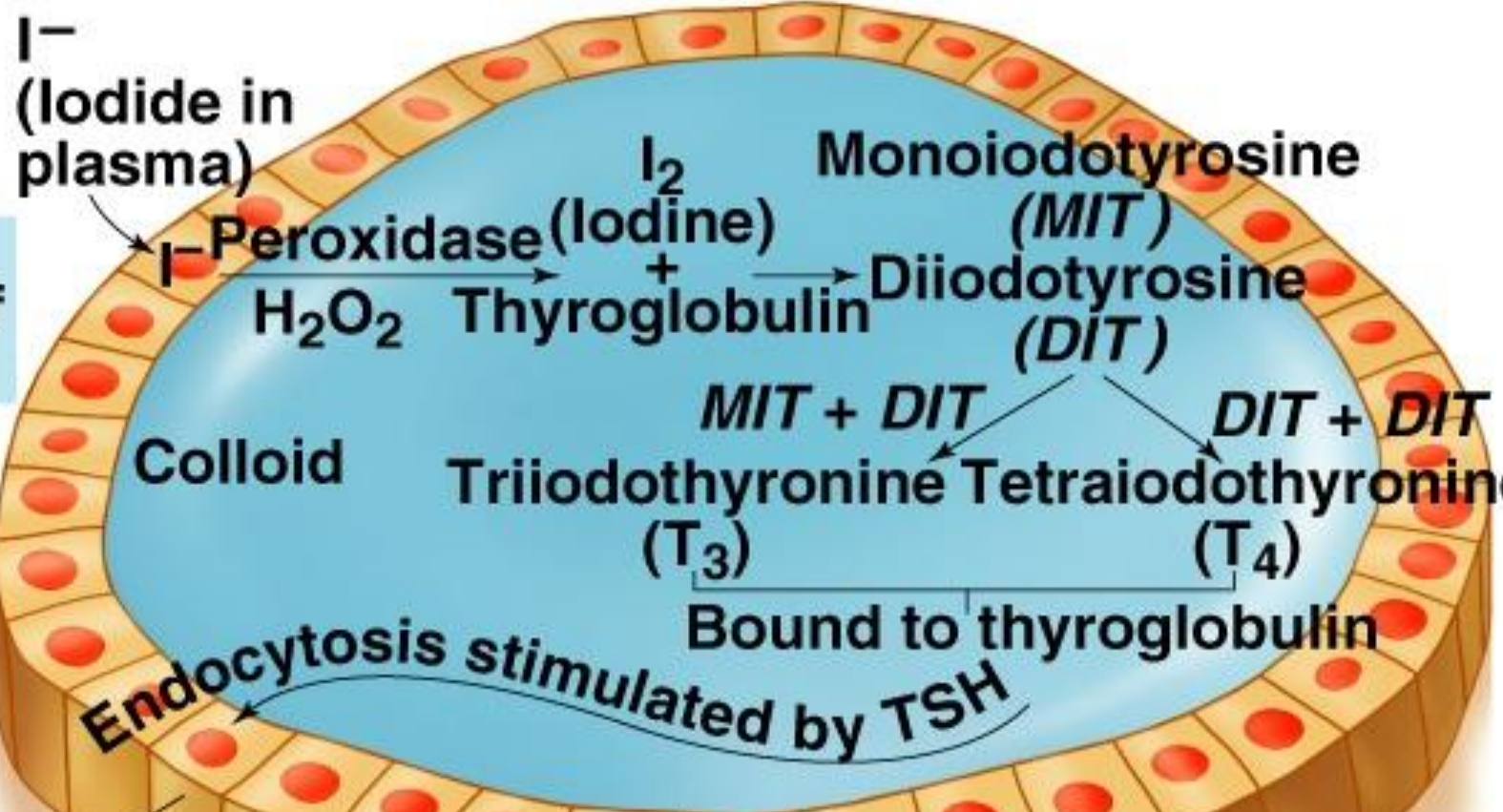
Follicular lumen





Blood plasma

Thyroid follicle



Thyroid uptake of iodide

Plasma carrier protein

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 remainder 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

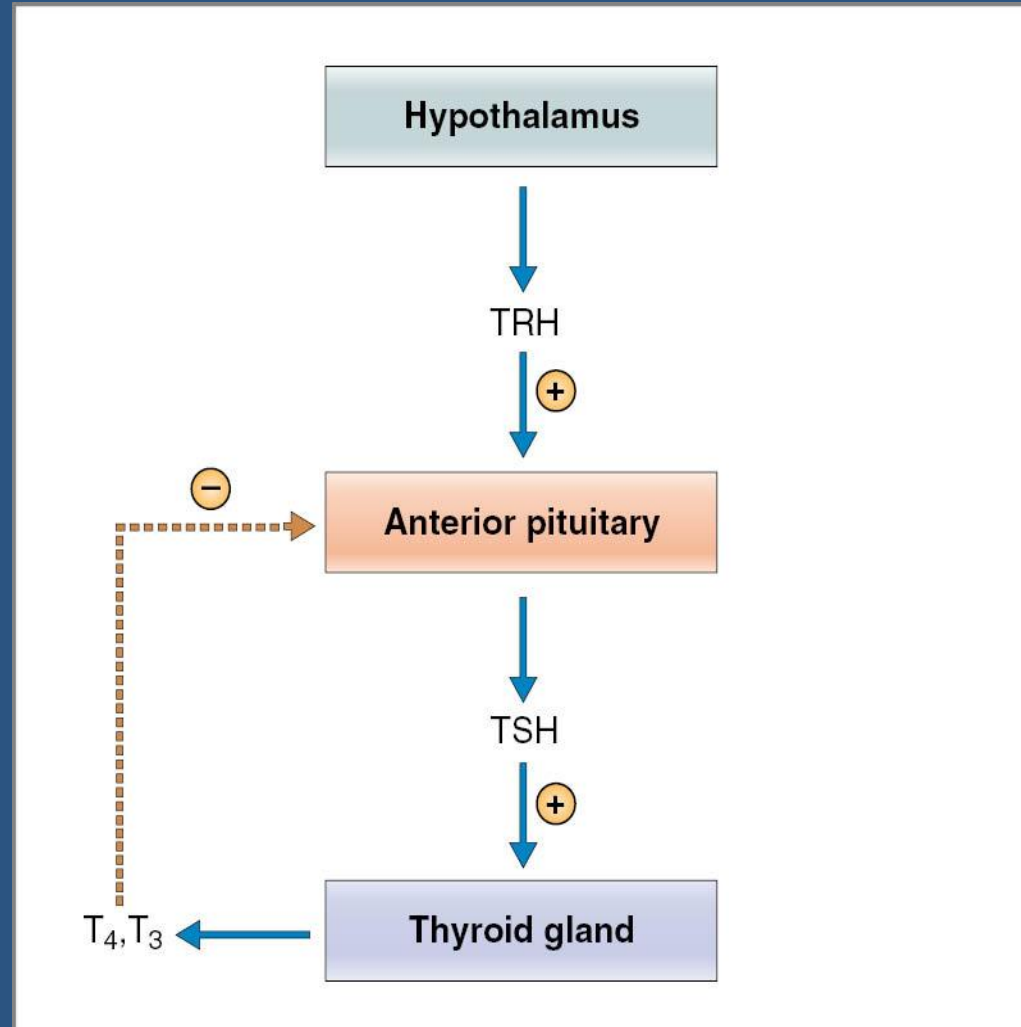
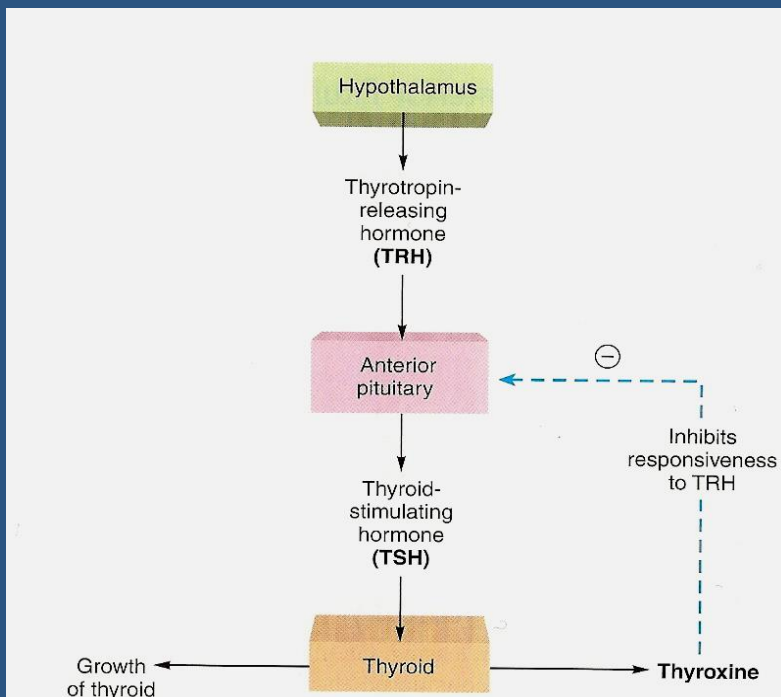
1. The release is slow because of the high affinity of the plasma binding proteins.
 - **$\frac{1}{2}$ of T4** in the blood is released every **6 days**.
 - **$\frac{1}{2}$ of T3** in the blood is released every **one day**.

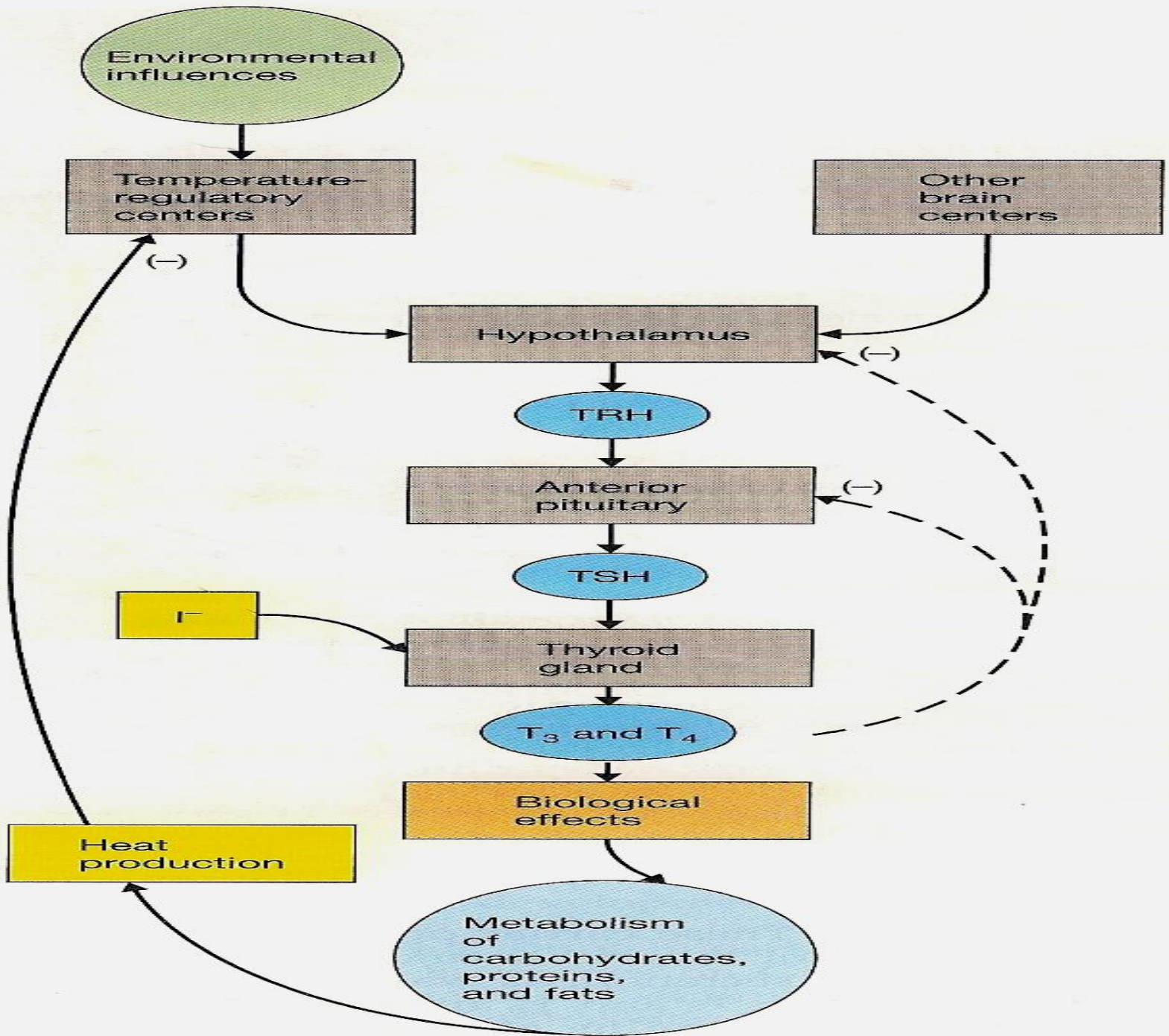
2- Stored in the targeted tissues .

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.

- **The metabolic effects are due to the induction of metabolic enzymes:**

- 1- cytochrome oxidase.**

- 2- NADPH cytochrome C reductase.**

- 3- alpha- glycerophosphate dehydrogenase.**

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.

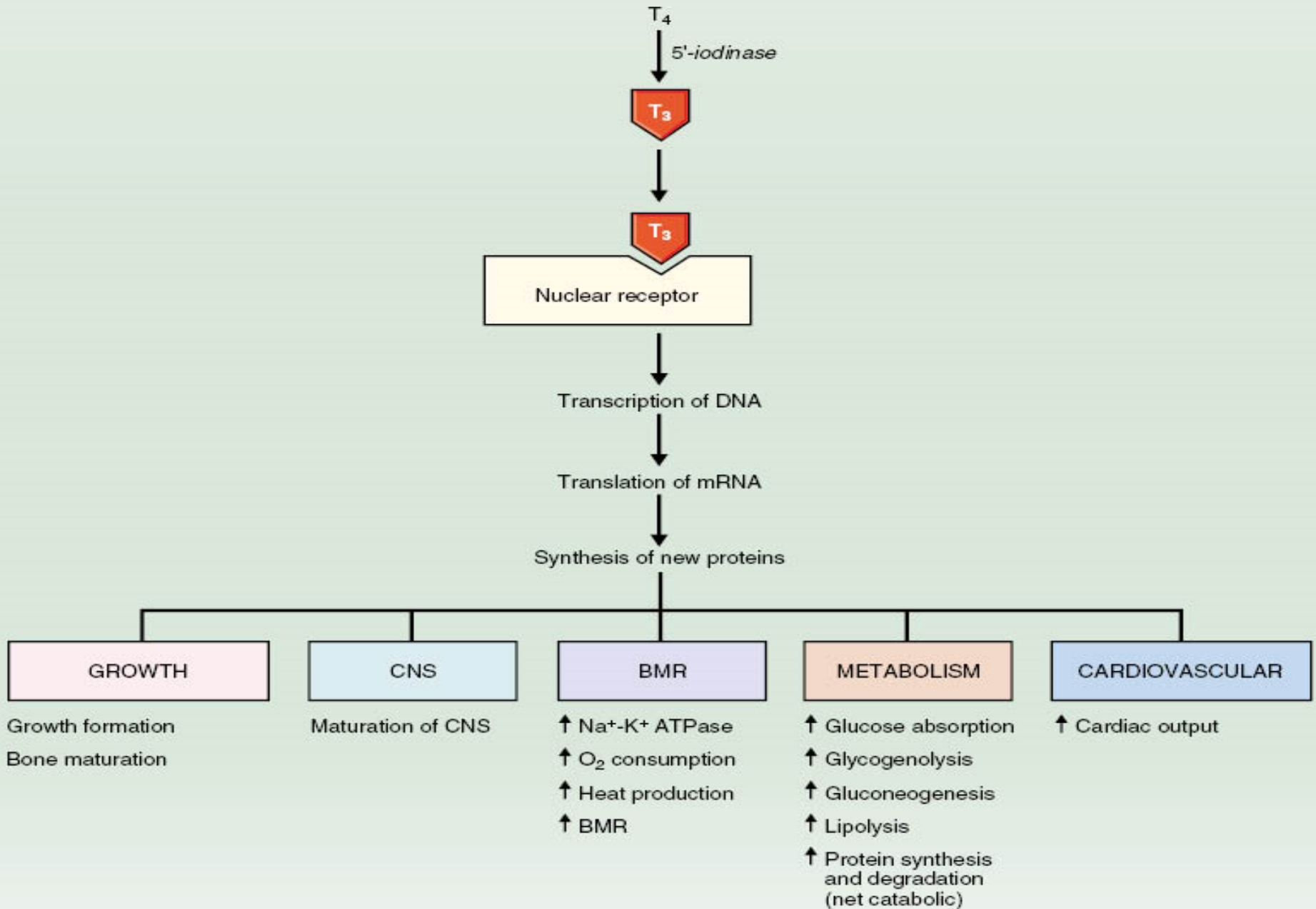
2- Increase of digestive juices secretion.

3- Increase of G.I tract motility.

excess secretion → diarrhea.

lack of secretion → constipation.

ACTIONS OF THYROID HORMONES



DISEASES OF THE THYROID GLAND

DR ABDULMAJEED AL-DREES

OBJECTIVES

- DESCRIBE PATHOPHYSIOLOGY BEHINED THE CAUSES OF HYPER-HYPOTHYROIDISM.
- DESCRIBE PATHOPHYSIOLOGY BEHINED THE SIGNS AND SYMPTOMS OF HYPER-HYPOTHYROIDISM.
- LIST THE TREATMENT

HYPERTHYROIDISM

- **Over activity of the thyroid gland.**
- **Women : men ratio (8:1).**
- **activity of gland :**
 - a)- **5- 10 times** increase in secretion.
 - b)- **2-3 times** increase in size.

CAUSES

1- Graves' disease :

- an autoimmune disorder.
- increased circulating level of **thyroid-stimulating immunoglobulins (TSI)**.
- 95%.
- **4 – 8** times more common in women than men.

2- Thyroid gland tumor:

- 95% is benign.

- history of head and neck irradiation and family history.

3- Exogenous T3 and T4:

(rarely cause)

4- Excess TSH secretion:

- diseases of the hypothalamus (TRH).**
- diseases of the pituitary (TSH).**

DIAGNOSIS

S+s :

1- Goiter in 95%.

2- skin:

- smooth, warm and moist.
- heat intolerance, night sweating.

3- musculoskeletal:

- Muscle atrophy.

4- Neurological:

- tremor.
- enhanced reflexes.
- irritability.

5- Cardiovascular:

- increase heart rate.
- increase stroke volume.
- arrhythmias.
- hypertension.

6- G.I tract:

- weight loss.
- diarrhea.

7- Exophthalmos:

- **anxious staring expression.**
- **protrusion of eye balls.**

8- Others:

- **menstrual cycle disturbance.**



INVESTIGATIONS

1- Serum T3, T4 ,TSH measurement.

In primary hyperthyroidism:

high T3, T4 and low TSH .

In secondary hyperthyroidism:

high T3, T4 and high TSH.

TREATMENT

1- Medical therapy:

- with 3-4 monthly monitoring.

2- Surgery:

- **Subtotal thyroidectomy.**

- **Indication for surgery:**

- a)- Relapse after medical treatment.

- b)- Drug intolerance.

- c)- Cosmetic.

- d)- Suspected malignancy.

HYPOTHYROIDISM

Under activity of the thyroid gland

more in woman (30- 60 years).

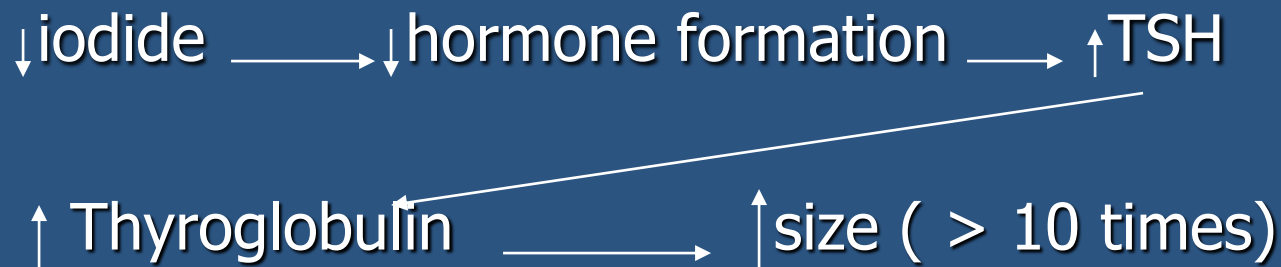
CAUSES

1- Inherited abnormalities of thyroid hormone synthesis :

- Peroxidase defect.
- Iodide trapping defect.
- Thyroglobulin defect.

2- Endemic Colloid Goiter:

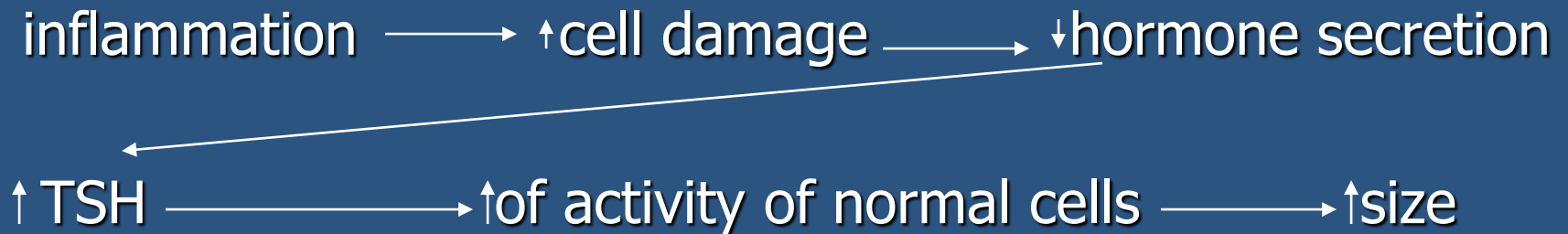
- before table salt.





3- Idiopathic Nontoxic Colloid Goiter:

- I intake is normal.
- **thyroiditis?**



4- Gland destruction (surgery).

5- Pituitary diseases or tumor.

6- Hypothalamus diseases or tumor.

DIAGNOSIS

1- skin :

- dry skin.
- cold intolerance.

2- Musculo skeletal:

- ↑ muscle bulk.
- ↓ in skeletal growth.
- muscle sluggishness

3- Neurological:

- **slow movement.**
- **impaired memory.**
- **decrease mental capacity.**

4- Cardiovascular:

- **heart rate**
- **stroke volume.**

5- G.I tract:

- constipation**
- increase weight.**

6- Myxoedema:

An edematous appearance throughout body.

7- others:

- loss of libido.**
- menstrual cycle disturbance.**



INVESTIGATIONS

1- Serum T3,T4 are low.

- TSH is elevated in primary.

**- TSH is low in secondary
hypothyroidism.**

TREATMENT

- **L- thyroxine**
- Starting dose is 25-50 μg .
- - At 2-4 weeks period.

The first response seen is the **weight loss.**



Table 9-9 Pathophysiology of Thyroid Hormones

	Hyperthyroidism	Hypothyroidism
Symptoms	<p>Increased basal metabolic rate</p> <p>Weight loss</p> <p>Negative nitrogen balance</p> <p>Increased heat production</p> <p>Sweating</p> <p>Increased cardiac output</p> <p>Dyspnea (shortness of breath)</p> <p>Tremor, muscle weakness</p> <p>Exophthalmos</p> <p>Goiter</p>	<p>Decreased basal metabolic rate</p> <p>Weight gain</p> <p>Positive nitrogen balance</p> <p>Decreased heat production</p> <p>Cold sensitivity</p> <p>Decreased cardiac output</p> <p>Hypoventilation</p> <p>Lethargy, mental slowness</p> <p>Drooping eyelids</p> <p>Myxedema</p> <p>Growth retardation</p> <p>Mental retardation (perinatal)</p> <p>Goiter</p>
Causes	<p>Graves' disease (increased thyroid-stimulating immunoglobulins)</p> <p>Thyroid neoplasm</p> <p>Excess TSH secretion</p> <p>Exogenous T₃ or T₄ (factitious)</p>	<p>Thyroiditis (autoimmune or Hashimoto's thyroiditis)</p> <p>Surgery for hyperthyroidism</p> <p>I⁻ deficiency</p> <p>Congenital (cretinism)</p> <p>Decreased TRH or TSH</p>
TSH Levels	<p>Decreased (feedback inhibition of T₃ on the anterior lobe)</p> <p>Increased (if defect is in anterior pituitary)</p>	<p>Increased (by negative feedback if primary defect is in thyroid gland)</p> <p>Decreased (if defect is in hypothalamus or anterior pituitary)</p>
Treatment	<p>Propylthiouracil (inhibits peroxidase enzyme and thyroid hormone synthesis)</p> <p>Thyroidectomy</p> <p>¹³¹I⁻ (destroys thyroid)</p> <p>β-Adrenergic blocking agents (adjunct therapy)</p>	<p>Thyroid hormone replacement therapy</p>

CRETINISM

Extreme hypothyroidism during infancy and childhood (failure of growth).

CAUSES

- 1- Congenital lack of thyroid gland (congenital cretinism).**
- 2- Genetic deficiency leading to failure to produce hormone.**
- 3- Iodine lack in the diet (endemic cretinism).**

SYMPTOMS

- 1- Infant is normal at birth but abnormality appears within weeks.**
- 2- Protruding tongue.**
- 3- Dwarf with short limbs.**
- 4- Mental retardation.**
- 5- Often umbilical hernia.**
- 6- teeth.**



TREATMENT

Changes are irreversible unless treatment is given early.



