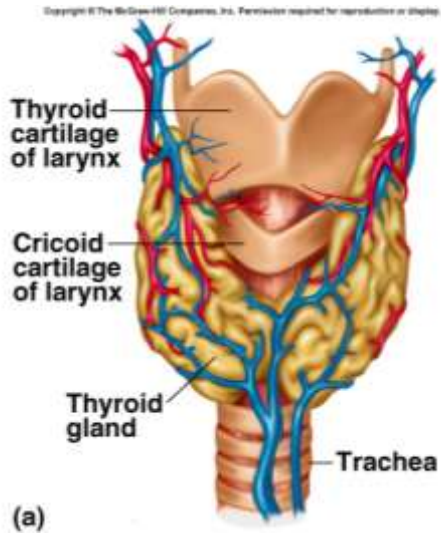


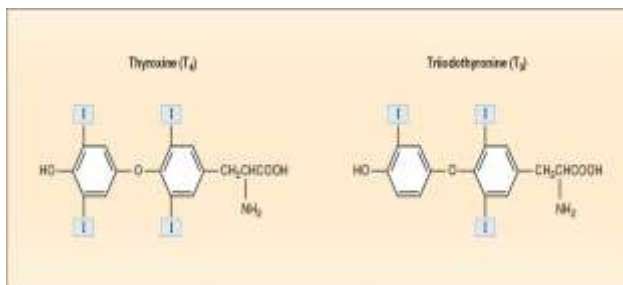
THE THYROID GLAND

- It is located below the larynx on either sides and anterior to the trachea.
- The first recognized endocrine gland.
- 20g in adult.



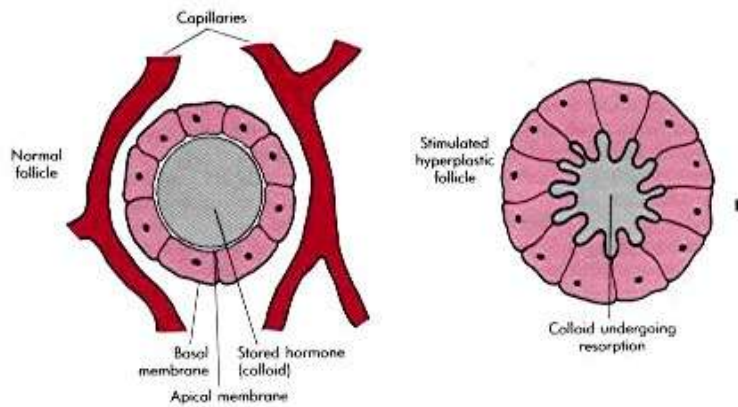
HORMONES:

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

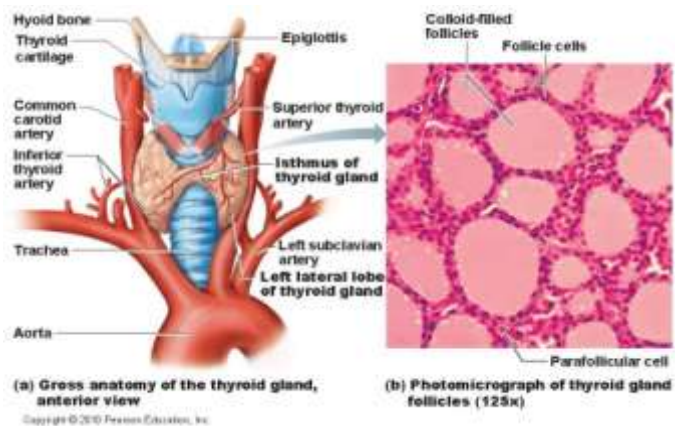


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SYNTHESIS:

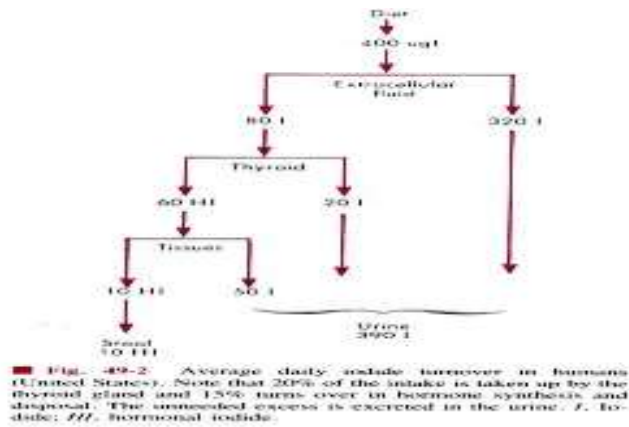


■ Fig. 49-1 A, Photomicrograph of thyroid gland follicle. B, Schematic drawing of normal thyroid gland follicle and a follicle stimulated by thyrotropin. Note change in shapes from cuboidal to columnar, relocation of nuclei to base of cells, and scalloped appearance of follicle lumen.



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.

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.

■ 4- ORGANIFICATION OF THYROGLOBULIN

■

■ Binding of iodine with Thyroglobulin.

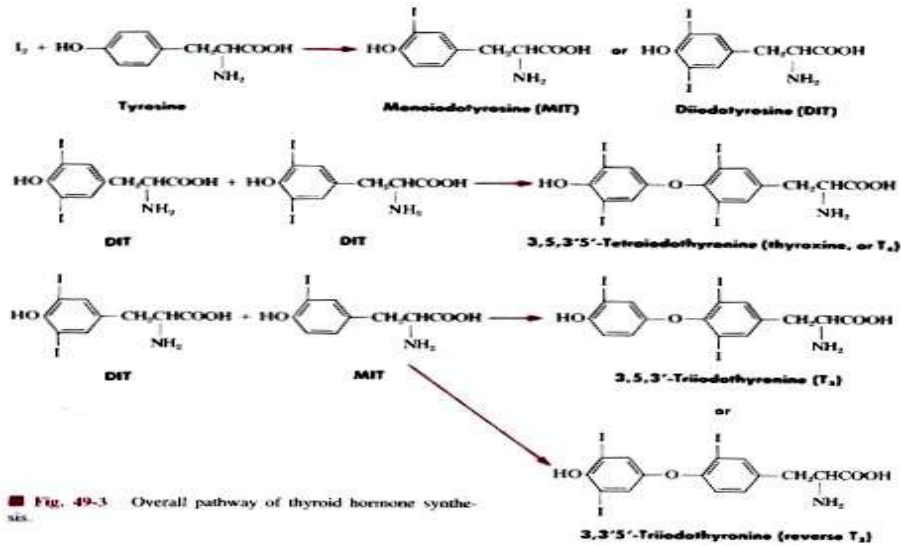
■ - Catalyzed by thyroid peroxidase.

MIT

DIT

■ - Remain attached to thyroglobulin until the gland stimulated to secret.

■ - It is located in or attached to the apical membrane.



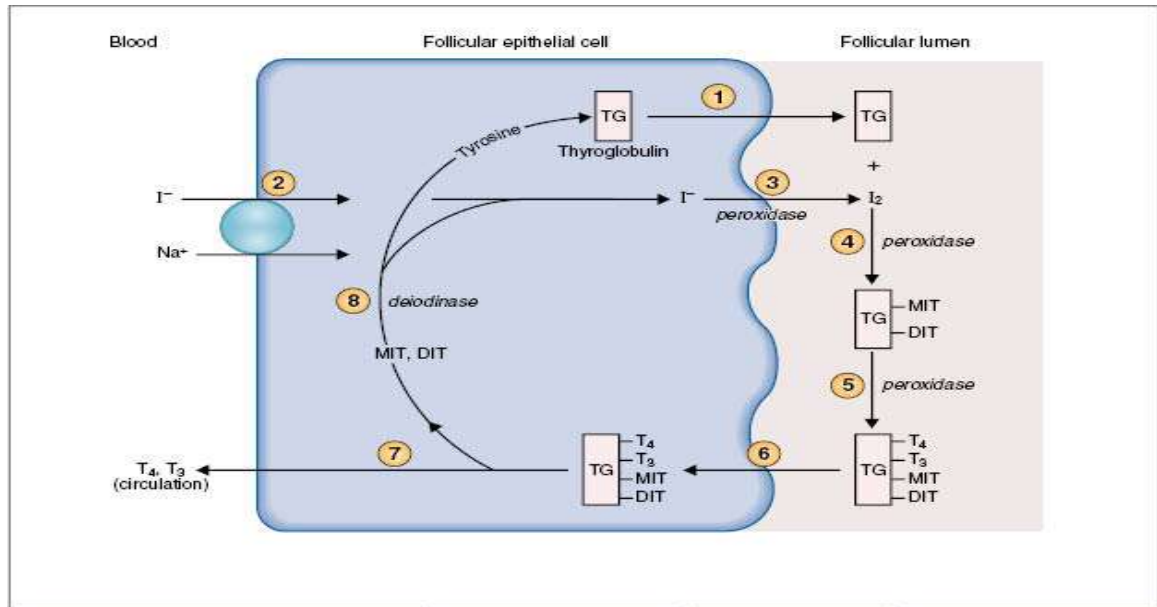
6- Endocytosis of thyroglobulin.

7- Fusion of lysosomes immediately with the vesicles.

8- Hydrolysis of the peptide bond to release $\text{DIT} + \text{MIT} + \text{T}_4 + \text{T}_3$ from the thyroglobulin.

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

10- Deiodination of DIT and MIT by thyroid deiodinase.



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	

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THYROID HORMONES IN THE CIRCULATION:

1- Unbound:

0.03% of T₄ and 0.3% of T₃.

2- Bound:

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

- The remainder is bound to albumine.

In hepatic failure:

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.

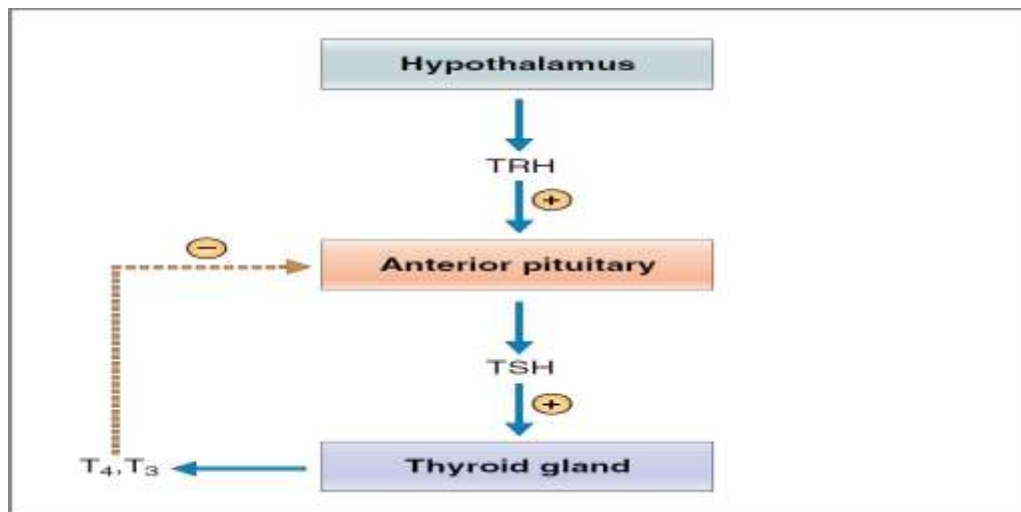
- $\frac{1}{2}$ of T3 in the blood is released every one day.

2- Stored in the targeted

tissues .

3- Enzyme 5- iodinase.

REGULATION OF HORMONES SECRETION:



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 metabolism , 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 (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.

4- malic enzymes.

5- several proteolytic enzymes

3- Effects on the cardiovascular system:

- increase heart rate.

- 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.**
- d)- myosine.**

6- Effects on the CNS:

A)- perinatal period:

Thyroid hormones are essential for maturation of the CNS.

perinatal decrease of hormones secretion

irreversible 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 catecholamines 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.

- 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.

