THYROID GLAND

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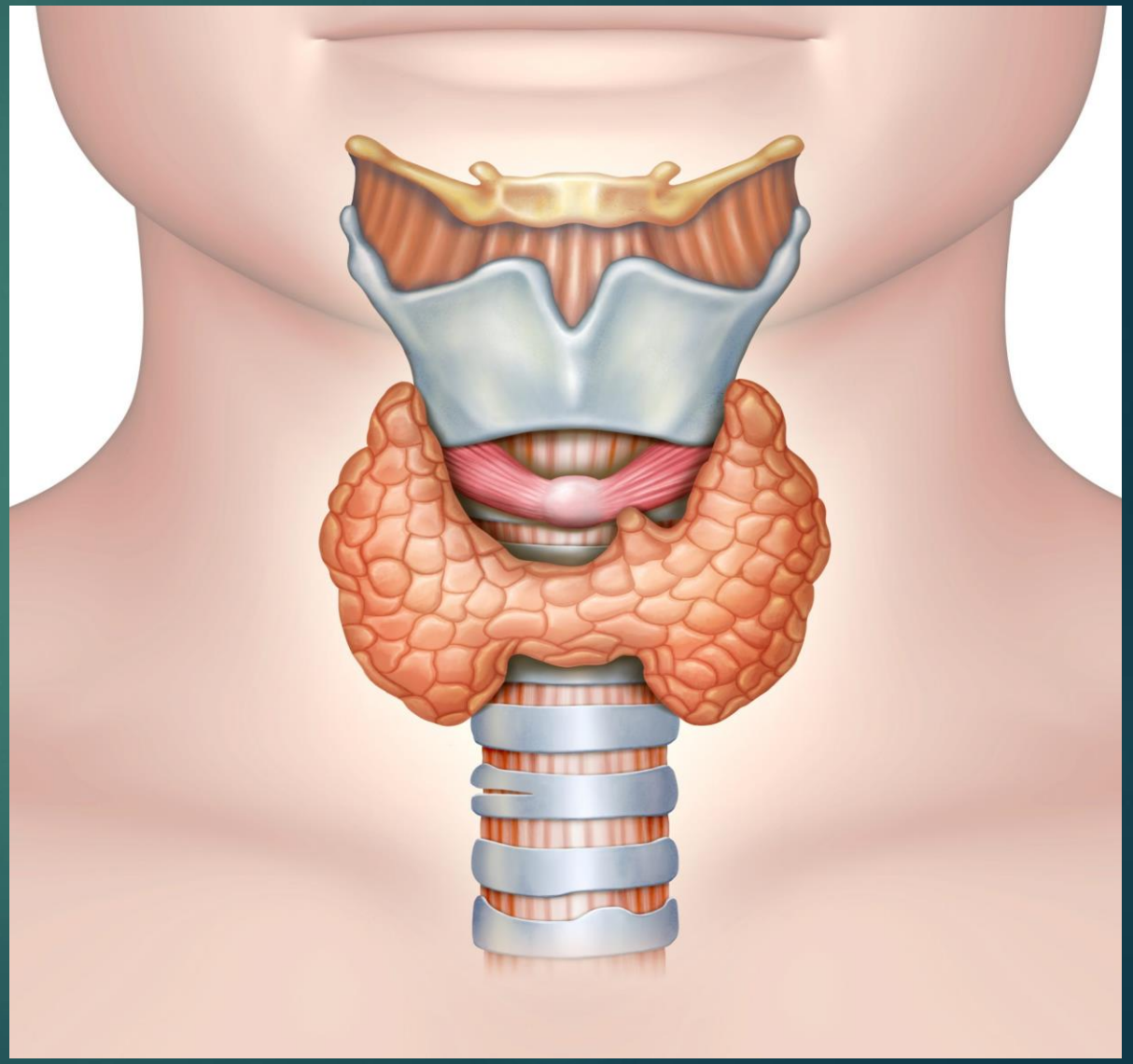
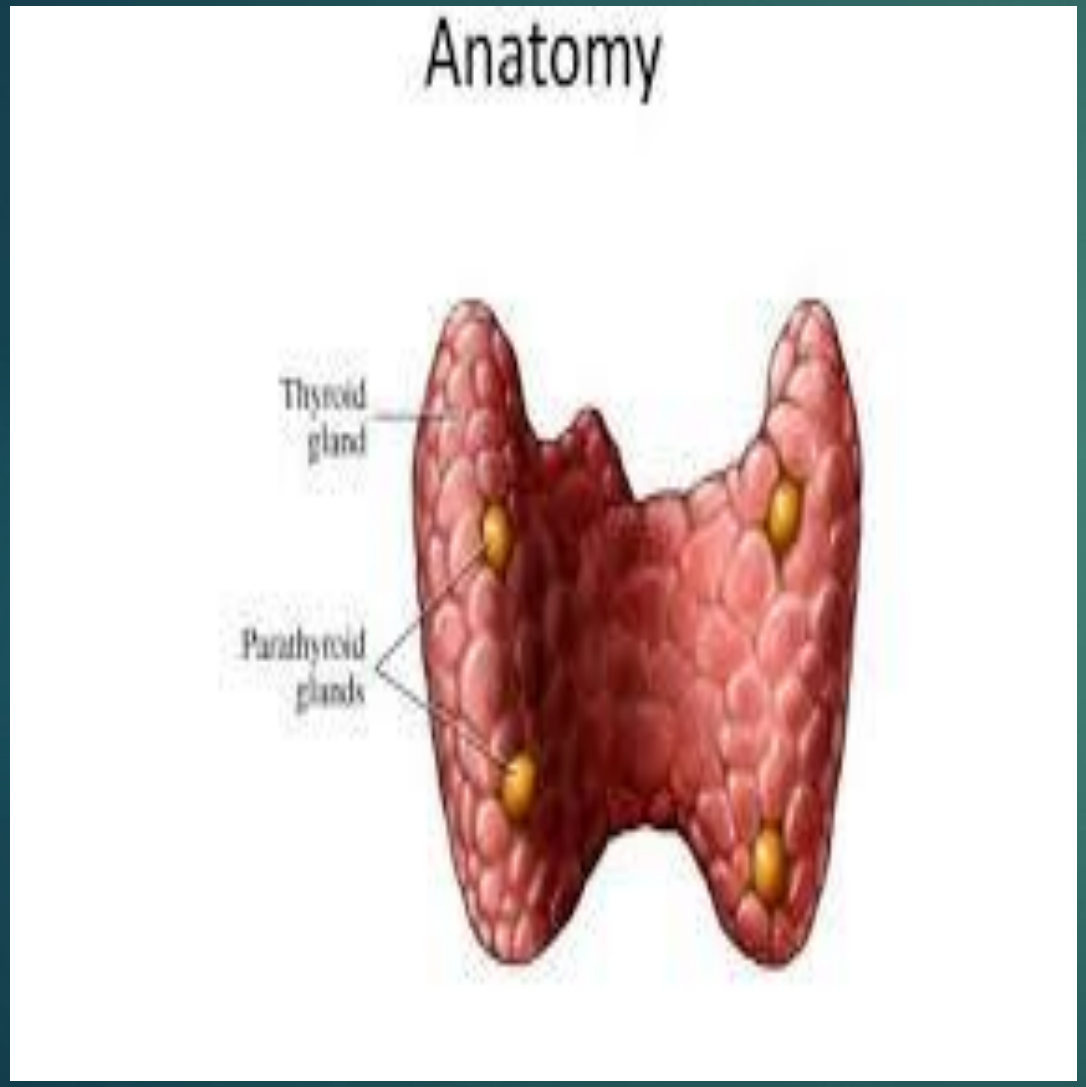
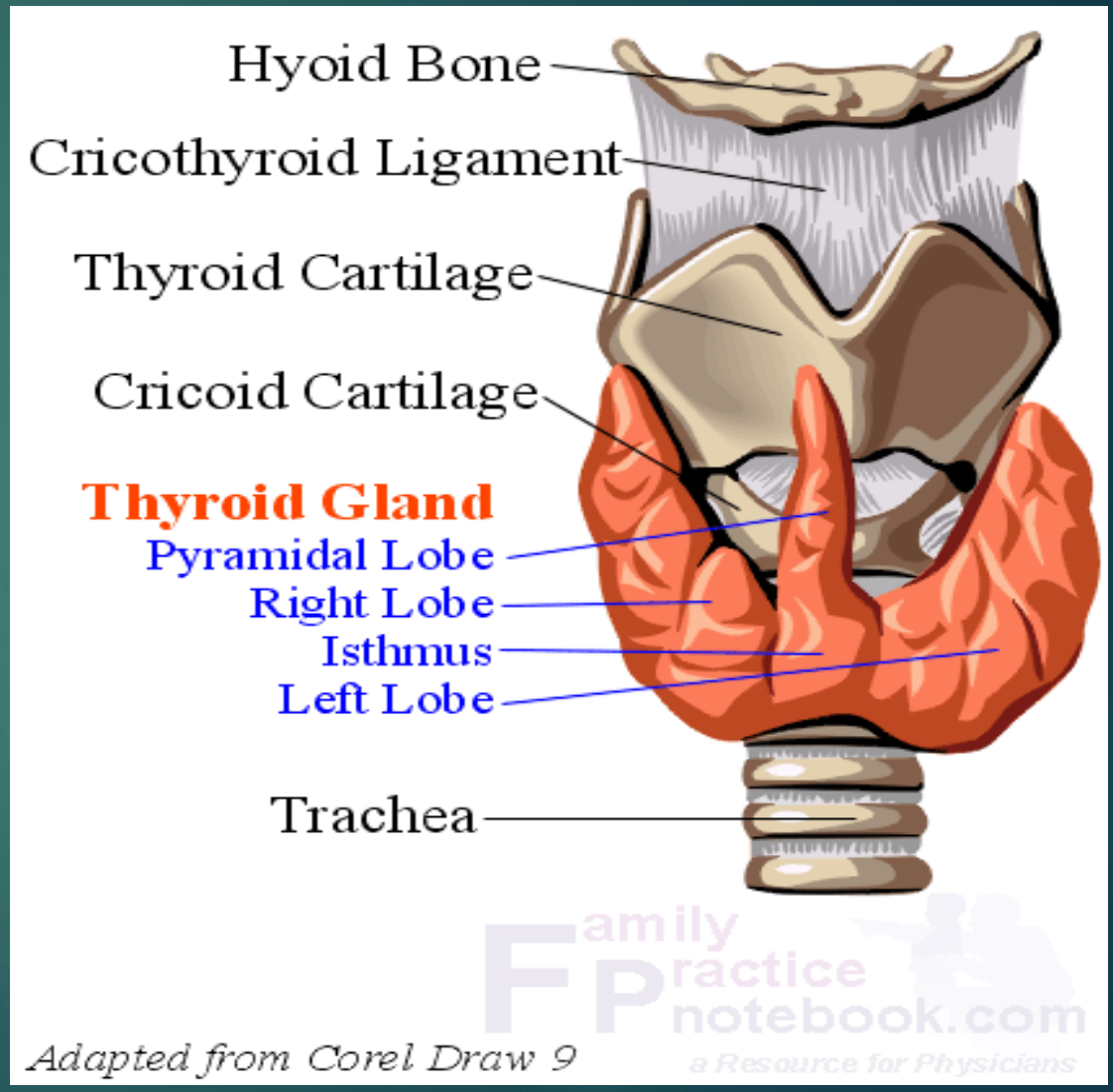


Learning objectives

- Anatomy of thyroid gland
- Synthesis of thyroid gland
- Inhibitors of thyroid gland synthesis
- Mechanism of action of thyroid gland
- Effects of thyroid gland
- Hypothroidism
- Hyperthyroidism

Anatomy of thyroid gland

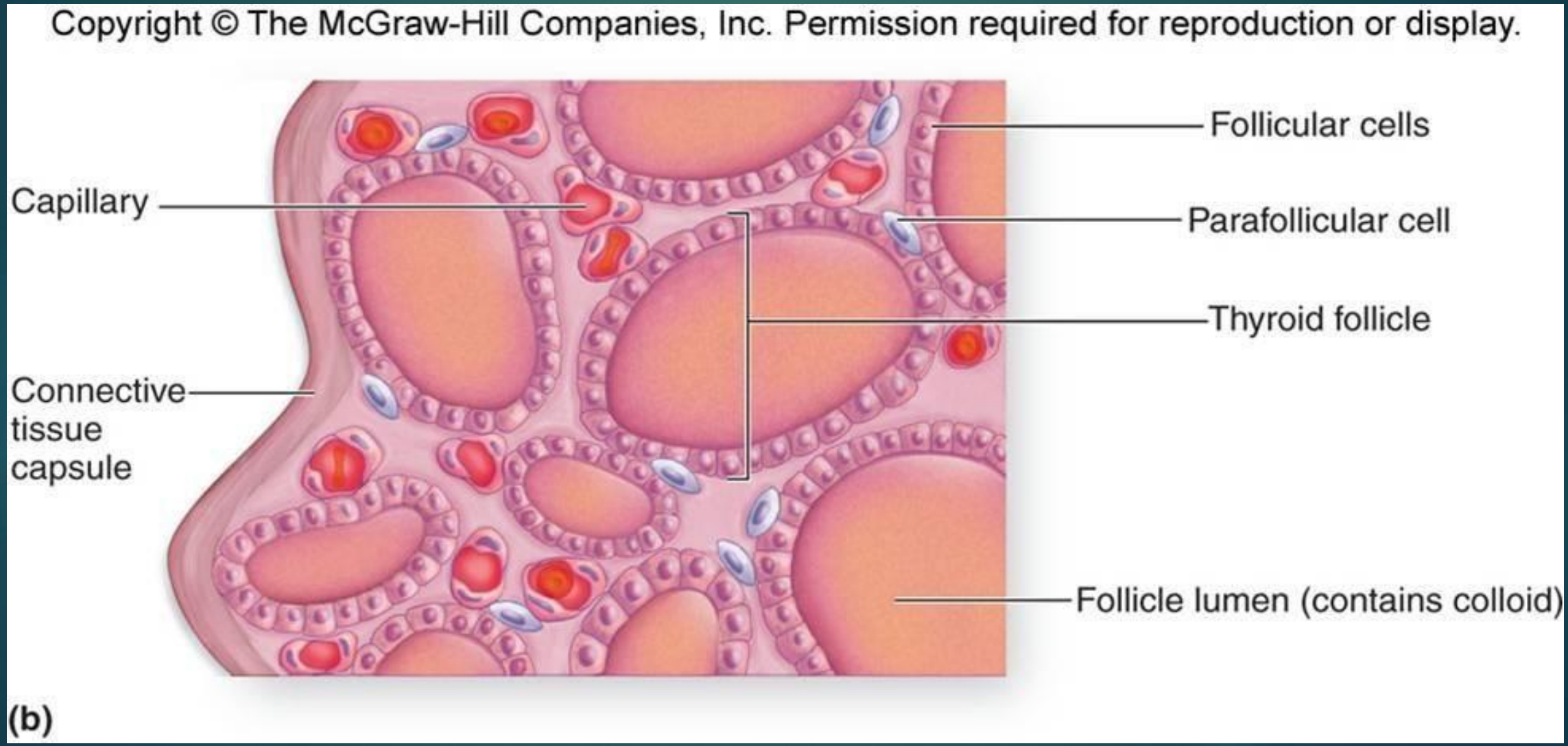




Histology of the Thyroid Gland

- The thyroid gland contains numerous follicles, composed of epithelial follicle cells and colloid.
- Also, between follicles are clear parafollicular cells, which produce calcitonin .

Histology



Thyroid Hormones

- There are two biologically active thyroid hormones:

  - tetraiodothyronine (T4; usually called thyroxine)

  - triiodothyronine (T3)

- Derived from modification of an amino acid (tyrosine)

Synthesis of thyroid harmones

- Two raw materials (substrates) required by thyroid gland to synthesize the thyroid hormones are:

1. Thyroglobulin
2. Iodine

- A. Thyroglobulin

Thyroid hormones are synthesised by the iodination of tyrosine residues of a large protein called "thyroglobulin".

Chemistry of thyroglobulin

- Thyroglobulin is a dimeric glycoprotein, with a molecular weight of 660,000.
- The receptor tyrosine molecules are present in the macroglobulin protein, each molecule containing 115 tyrosine residues.
- Carbohydrates - 8 to 10 per cent by weight of thyroglobulin and iodide for about 0.2 to1 per cent, depending on the iodine content of the diet.
- The carbohydrates are N-acetyl glucosamine,mannose, glucose, galactose, fucose and sialic acid.

When Iodine supplies is sufficient, T4 : T3 ratio is about7:1. In iodine deficiency, this ratio decreases, including the MIT/DIT ratio. T3 and T4 after being synthesised,remains in the bound form until it is secreted. When they are secreted, the peptide bonds are hydrolysed and free T3 and T4 enter the thyroid cells, cross them and are discharged into the capillaries.

Iodine

- Thyroid hormones are unique biological molecules in that they incorporate iodine in their structure.
- Thus, adequate iodine intake (diet, water) is required for normal thyroid hormone production.
- Major sources of iodine:
  - iodized salt
  - iodated bread
  - dairy products
- Minimum requirement: 75 micrograms/day

SYNTHESIS OF T3 & T4:

- T3& T4 are synthesized in follicular cells.

1. The steps are:

A. Iodine Trapping/Transportation
B. Oxidation
C. Organification
D. Coupling
E. Hydrolysis

1) IODIDE TRAPPING / TRANSPORTATION:

Moves iodide from extracellular space to follicular cells.

There , iodide is trapped with the help of transport protein and the enzymes are Na+ ATPase and K+ ATPase.

2) OXIDATION (OF IODIDES):

Conversion of iodide into iodonium with the help of enzyme peroxidase.

3) ORGANIFICATION:

- IODONIUM binds to Tgb, OR
- Thyroglobulin is released into the colloid space, where it's tyrosine residues are iodinated by I^+.
- This results in monoiodotyrosine (MIT) or diiodotyrosine (DIT
- and MIT& DIT are formed

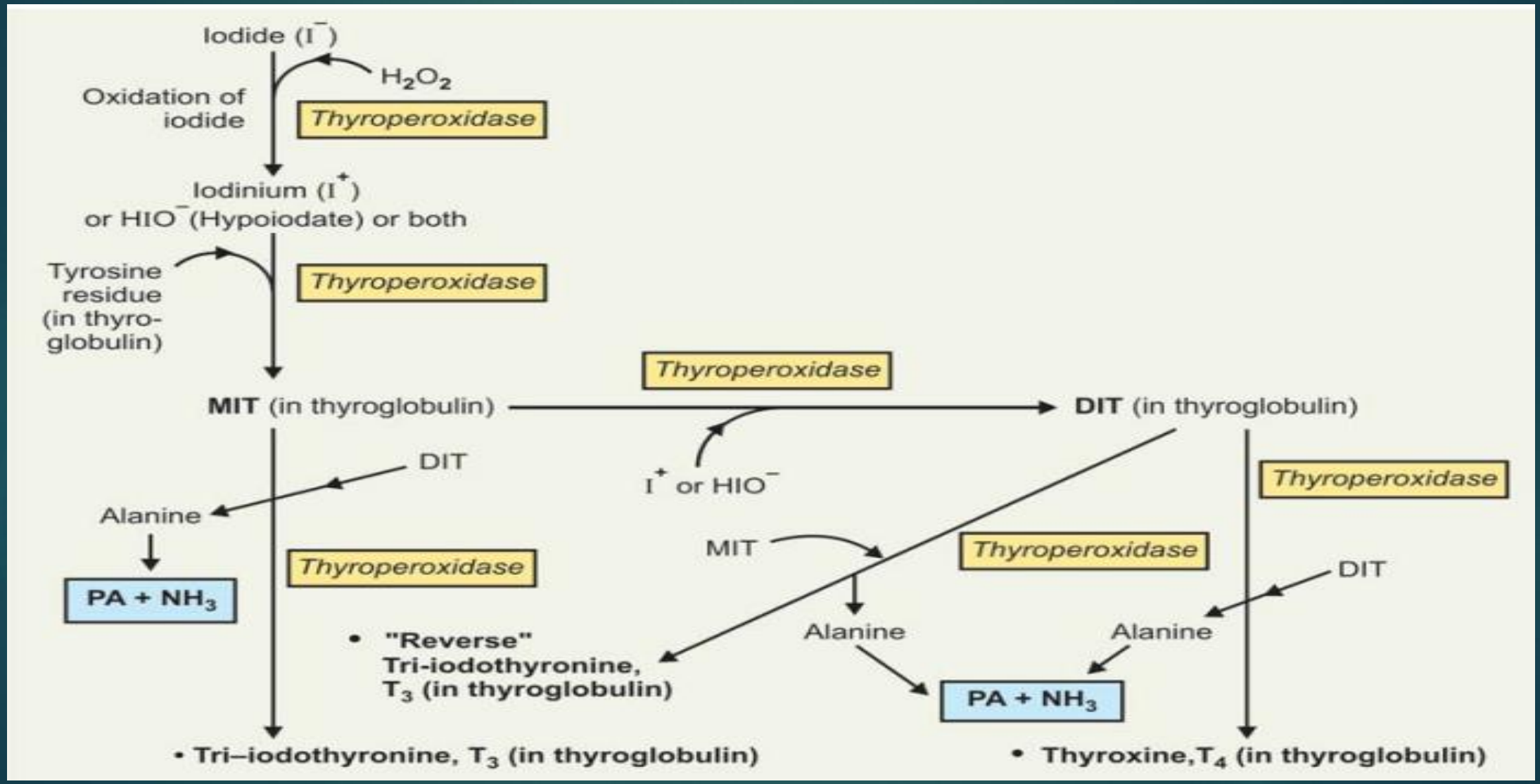
4)COUPLING:

- Binds DIT + DIT to form→ T4
- Binds DIT + MIT to form → T3

5) HYDROLYSIS:

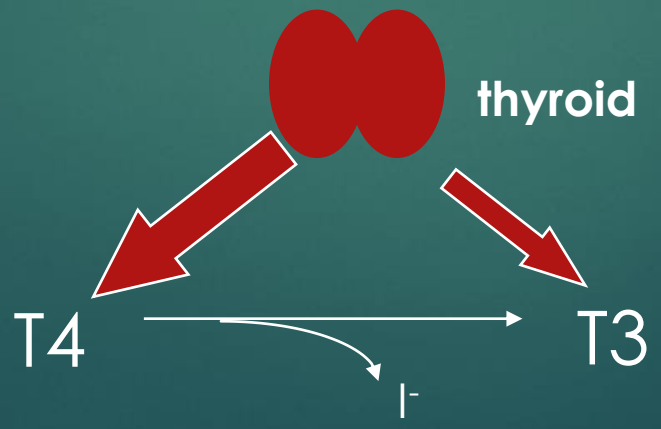
- Phagocytosis occurs and phagosomes fuses with lysosomes to form phagolysosomes.
- And than hydrolysis occurs by proteases and peptidases tp relase T3 AND T4 in the plasma , but in protein bound iodide form.

Biosynthesis of thyroid harmones



Differences between T4 and T3

- The thyroid secretes about 80 micrograms of T4, but only 5 micrograms of T3 per day.
- However, T3 has a much greater biological activity (about 10X) than T4.
- An additional 25 micrograms/day of T3 is produced by peripheral monodeiodination of T4.



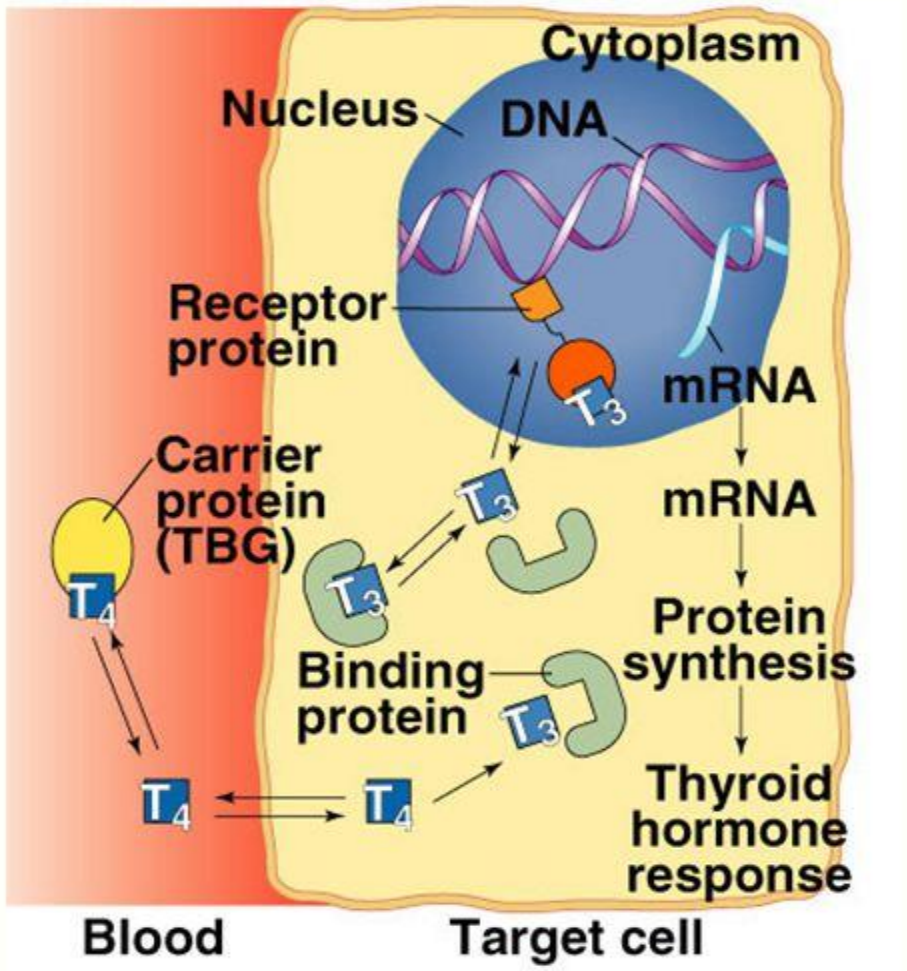
INHIBITORS:

1. Perchlorate
2. Pertachnetate — INHIBITS TRAPPING
3. Perhenate

1.Thiourea
2.Methamizole — INHIBITS OXIDATION
3. Thiouracil

1) Potassium iodide — INHIBITS HYDROLYSIS

Thyroid hormones
Mechanism of action



- T4 and T3 must dissociate from thyroxine binding globulin (TBG) in plasma before entering into the cells.
- In the cells, T4 is deiodinated to **T3** that enters nucleus and attaches to specific receptors which promotes mRNA and protein synthesis.

Mechanism of action of thyroid hormones

- T4 and T3 are dissociated from thyroid binding globulin & enters into cells
- In the cells,
  - T4 is enzymatically deiodinated to T3
  - T3 enters into nucleus and attaches to the specific receptors,
  - In nucleus, T3 promotes mRNA formation and protein synthesis (slow response).
  - Proteins produces the response

Effects of Thyroid Hormone on Nutrient Sources

Effects on carbohydrates:

low doses of thyroid hormone increase glycogen synthesis (low metabolic rate; storage of energy)

- high doses increase glycogen (high rate; glucose production)

Effects on Lipids:

Increased thyroid hormone levels stimulate fat mobilization, leading to increased concentrations of fatty acids in plasma.

They also enhance oxidation of fatty acids in many tissues.

Finally, **plasma concentrations of cholesterol and triglycerides are inversely correlated with TH levels.**

Cardiovascular system:

Thyroid hormones increases heart rate, cardiac contractility and cardiac output.

They also promote vasodilation, which leads to enhanced blood flow to many organs.

Central nervous system

Both decreased and increased concentrations of thyroid hormones lead to alterations in mental state. Individual tends to feel mentally sluggish in decrease TH level, while increase induces anxiety and nervousness.

Reproductive system

Normal reproductive behavior and physiology is dependent on having essentially normal levels of thyroid hormone.

Hypothyroidism in particular is commonly associated with infertility.

Specific actions of thyroid hormone:development

- TH is critical for normal development of the skeletal system and musculature.
- TH is also essential for normal brain development and regulates synaptogenesis, neuronal integration, myelination and cell migration.
- **Cretinism** is a condition of severely stunted physical and mental growth due to untreated congenital deficiency of thyroid hormones (congenital hypothyroidism) due to maternal nutritional deficiency of iodine.

On vitamins

- Administration of large amounts of thyroid hormones increase the requirement of certain members of vitamin B-complex (thiamine, pyridoxine,pantothenic acid) and for vitamin C - presumably related to the stimulation of oxidative and catabolic processes.

- Thyroxine is necessary for hepatic conversion of carotene to vitamin A and the accumulation of carotene in the bloodstream (“carotinaemia”) in hypothyroidism is responsible for yellowish tint of the skin.

Thyroid Hormone Deficiency: Hypothyroidism

- Early onset: delayed/incomplete physical and mental development
- Later onset (youth): Impaired physical growth
- Adult onset (myxedema) : gradual changes occur. Tiredness, lethargy, decreased metabolic rate, slowing of mental function and motor activity, cold intolerance, weight gain, goiter, hair loss, dry skin. Eventually may result in coma.
- Many causes (insufficient iodine, lack of thyroid gland, lack of hormone receptors, lack of TBG….)

GOITER:

- It is the swelling of thyroid gland and is also known as endemic goiter.
- It is of two types:

1. Simple goiter (deficiency of hormone)
2. Toxic goiter (excess of hormone)

1) Simple goiter:

- It is and enlargement of thyroid gland.
- Patients does not show any signs of excessive thyroid activity
- It is due to the deficiency of thyroid hormone,

2) TOXIC GOITER:

- IN toxic goiter the enlarged thyroid gland secrets an excess of thyroid hormone and the patient is

1. Nervous
2. Looses weight
3. Tremors and palpitations
4. Increased BP
5. Exophthalamus

Thyroid Hormone Excess: Hyperthyroidism

- Emotional symptoms (nervousness, irritability), fatigue, heat intolerance, elevated metabolic rate, weight loss, tachycardia, goiter, muscle wasting, apparent bulging of eyes, may develop congestive heart failure.
- Also due to many causes (excessive TSH release, autoimmune disorders,…)

Graves' disease:

condition usually caused by excessive production of thyroid hormone and characterized by an enlarged thyroid gland, protrusion of the eyeballs, a rapid heartbeat, and nervous excitability. Also called exophthalmic goiter.

EXAMPLES OF THYROID DISEASES

Hypothyroidism

Hyperthyroidism

Sources ;

- Chatterjea
- Google images