Thyroid Hormones 2

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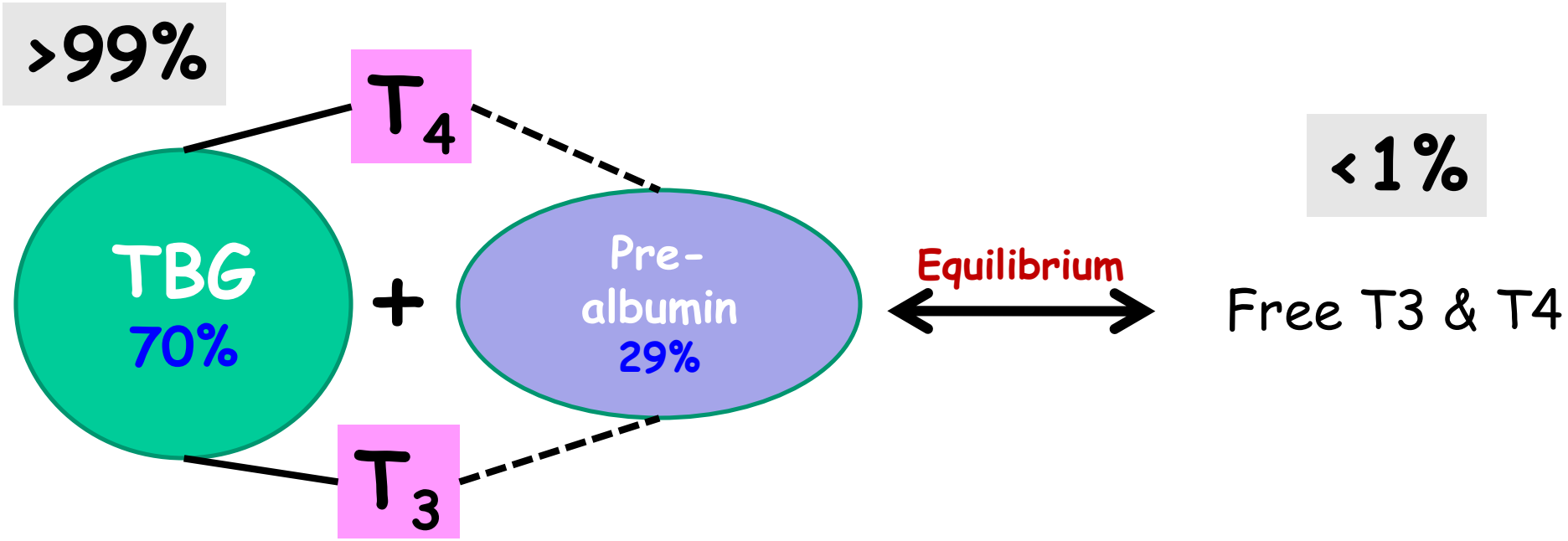
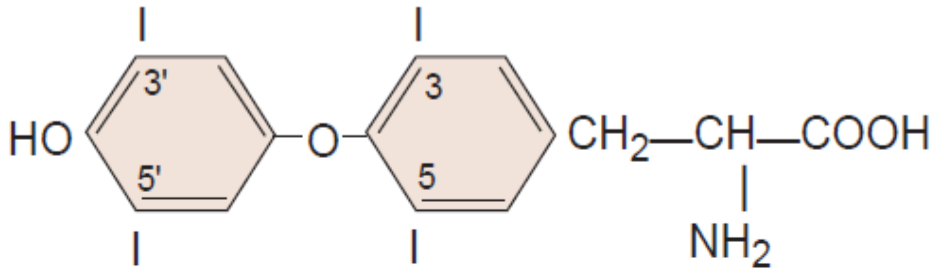
Transport of thyroid hormones by blood



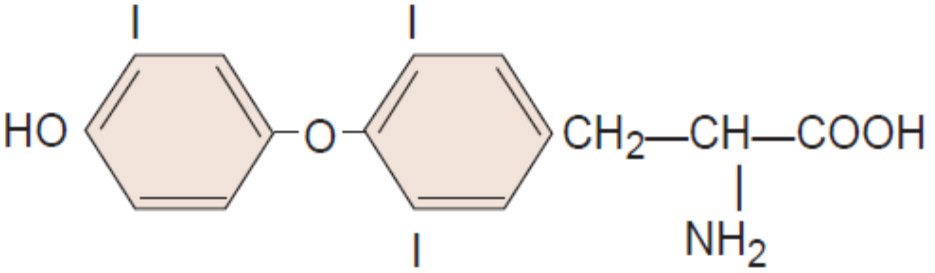
- T4 has the higher affinity **(10 times)** for binding proteins; therefore, it binds more tightly to protein than does T3, and consequently has a greater half-life than T3.
- Phenytoin sodium and salicylates compete with T3 & T4 for binding to TBG.

Structure of Thyroid Hormnes

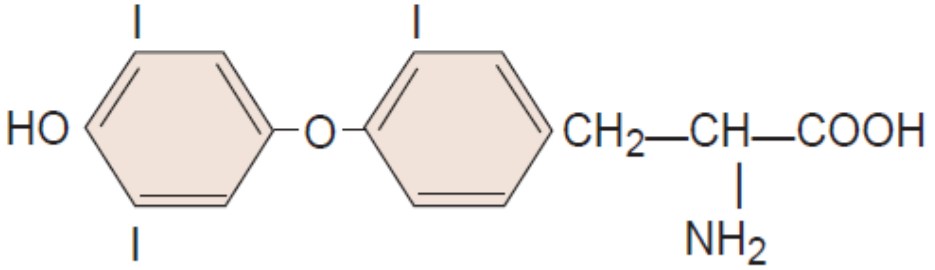


Thyroxine (T_4) 3,5,3',5',-tetra-iodothyronine

Outer phenol ring



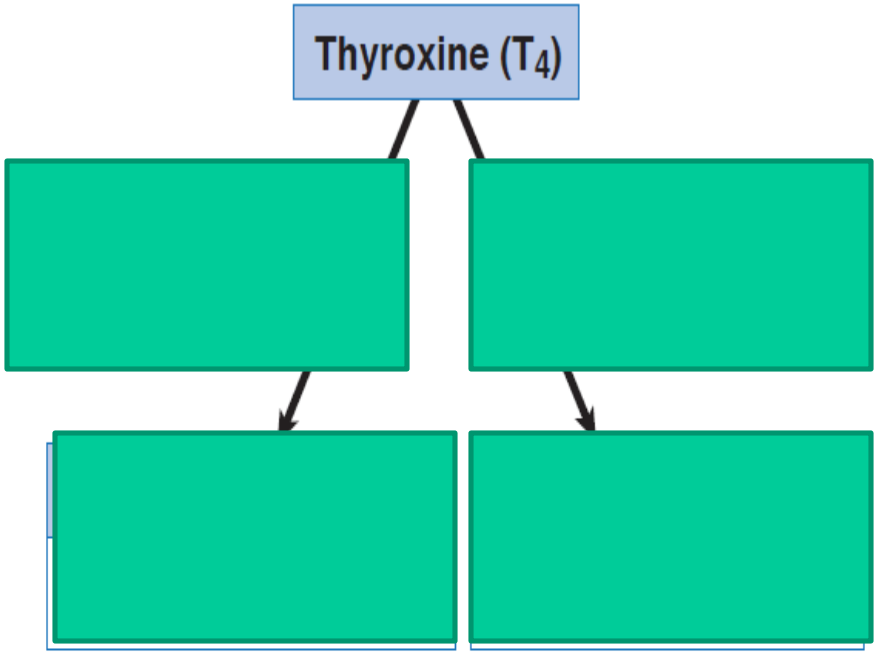
3,5,3'-tri-iodothyronine (T_3)
- More active form of hormone
- No 5' I



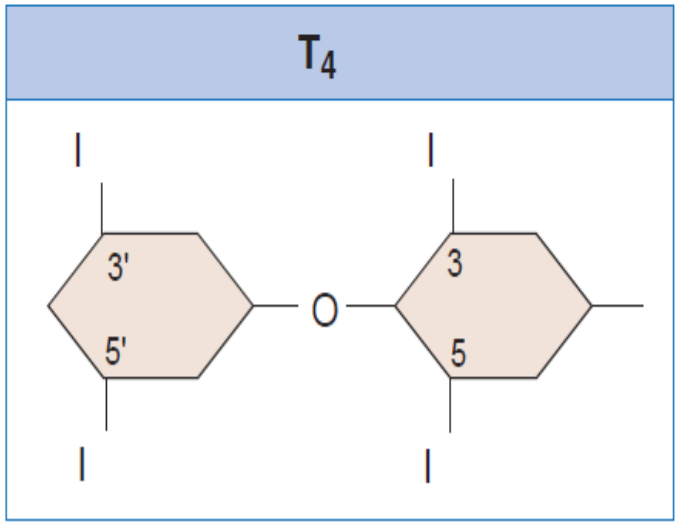
3,3',5'-tri-iodothyronine (reverse T_3)
- No activity
- No 5 I

Peripheral conversion of Thyroid Hormones

- Many target tissues can regulate the conversion of T4 to either T3 or **rT3**, thereby locally controlling hormone activity.
- Depends on tissue need



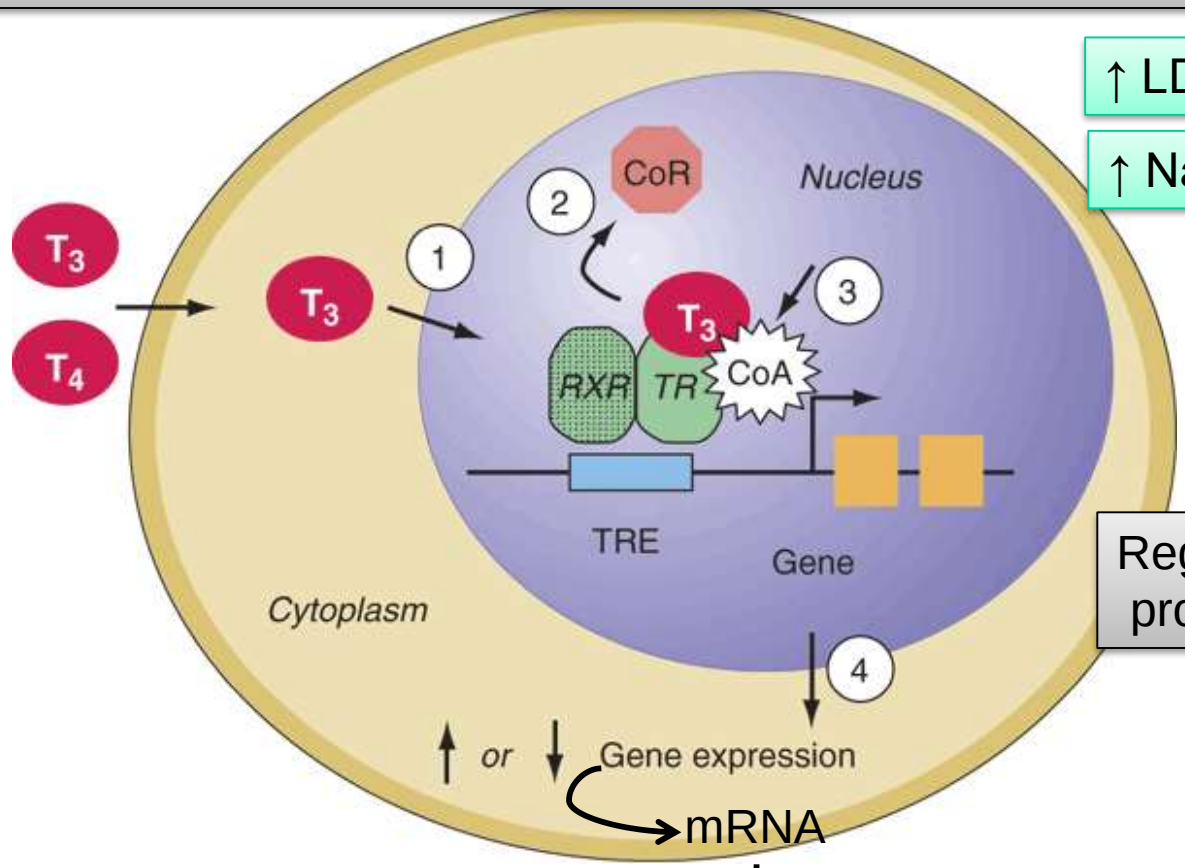
- Most of the circulating T3 is derived from the peripheral conversion of T4 into T3 and its release again into the circulation (e.g., liver, kidney, and skeletal muscle).



ormone action

Free thyroid hormone receptor (TR) binds to hormone response element (HRE) and corepressor (CoR)

After binding to receptor, CoR is liberated and coactivators (CoA) is bound and the transcription to mRNA begins



↑ LDL receptor in liver

↑ Na- K ATP-ase in each cell

↑ Growth

↑ Metabolism

Regulatory proteins

structural proteins

Functional proteins

mRNA

Metaboloic actions of Thyroid Hormone

- Exerts its actions on every cell of the body
  - Increases metabolism
  - Increases BMR
  - Increases β-adrenergic drive (↑ expression of β receptors)
- under normal conditions (normal conc.),
  - Anabolic
    - Bcz its protein synthesis effect is more
- All the effects are due to Protein synthesis
  - Increased expression of proteins by thyroid hormones

Metaboloic actions of Thyroid Hormone

1. Effect on CHO metabolism
   - Increased utilization of glucose
     - Increasing the absorption of glucose by intestine
       - by increased synthesis of transporters
     - Increased glycolysis
       - By increasing the synthesis of the enzymes of the pathway
     - Increased glycyogenolysis
     - Increased GN
       - By increased β_2 receptors on hepatocytes

Metaboloic actions of Thyroid Hormone

2. Effect on fat metabolism

- Increased mobilization of fats from adipose tissues; causing
  - Increased fat mobilization
    - by increased expression β_3 receptor on adipocytes.
  - Increased fFA conc in plasma
- Decreases plasma cholesterol conc
  - Increased LDL receptor synthesis

Metaboloic actions of Thyroid Hormone

3. Effect on protein synthesis and turn over
   - Enzymes for protein degradation are expressed

4. Effect on Nitrogen metabolism
   - Depend on food intake especially protiens
   - If food intake is not increased, endogenous proteins are catobolized and weight is lost
     - Enzymes responsible for proteins catabolism are expressed

- So both catabolic and anabolic

Metaboloic actions of Thyroid Hormone

5. Effect on vitamin metabolism

- Need for vitamins is increased; bcz
  - Enzymes synthesis increased
- Coenzyme requirement also increased
- vitamin deficiency syndromes may be precipitated.

Metaboloic actions of Thyroid Hormone

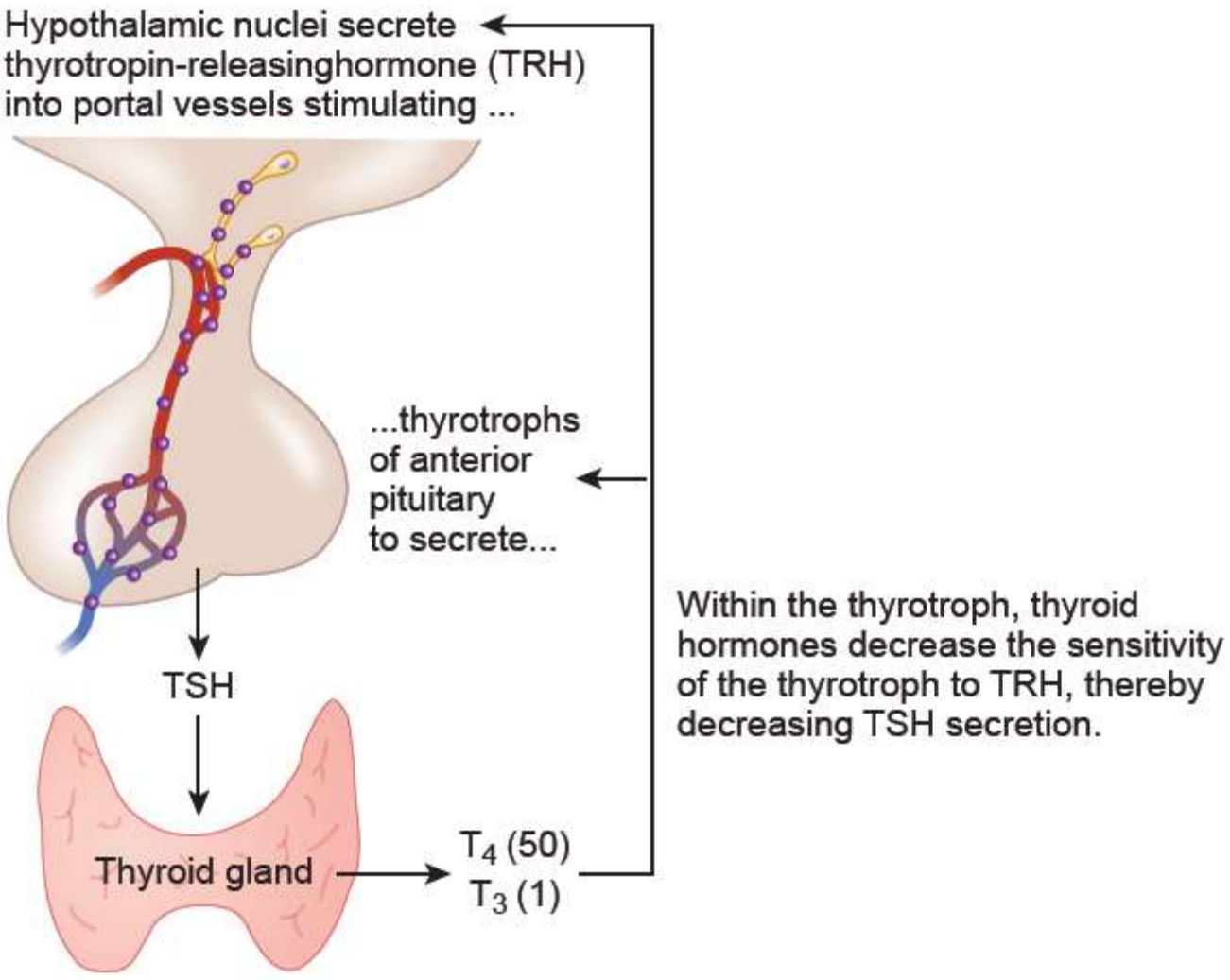
6. Increases Oxygen consumption
   - By increasing the synthesis of enzymes of ETC
     - Leading to increased respiration
       - Coupled to phosphorylation
         - » So increased ATP production
           - » More heat is dissipated
             - » Which is the mechanism of thermogenesis by thyroid hormones
               - » Also TH leads to synthesis of uncouplers

Metaboloic actions of Thyroid Hormone

7. Effect on ATP

- Increased synthesis
- Increased consumption of ATP
  - increased synthesis of various ATPase

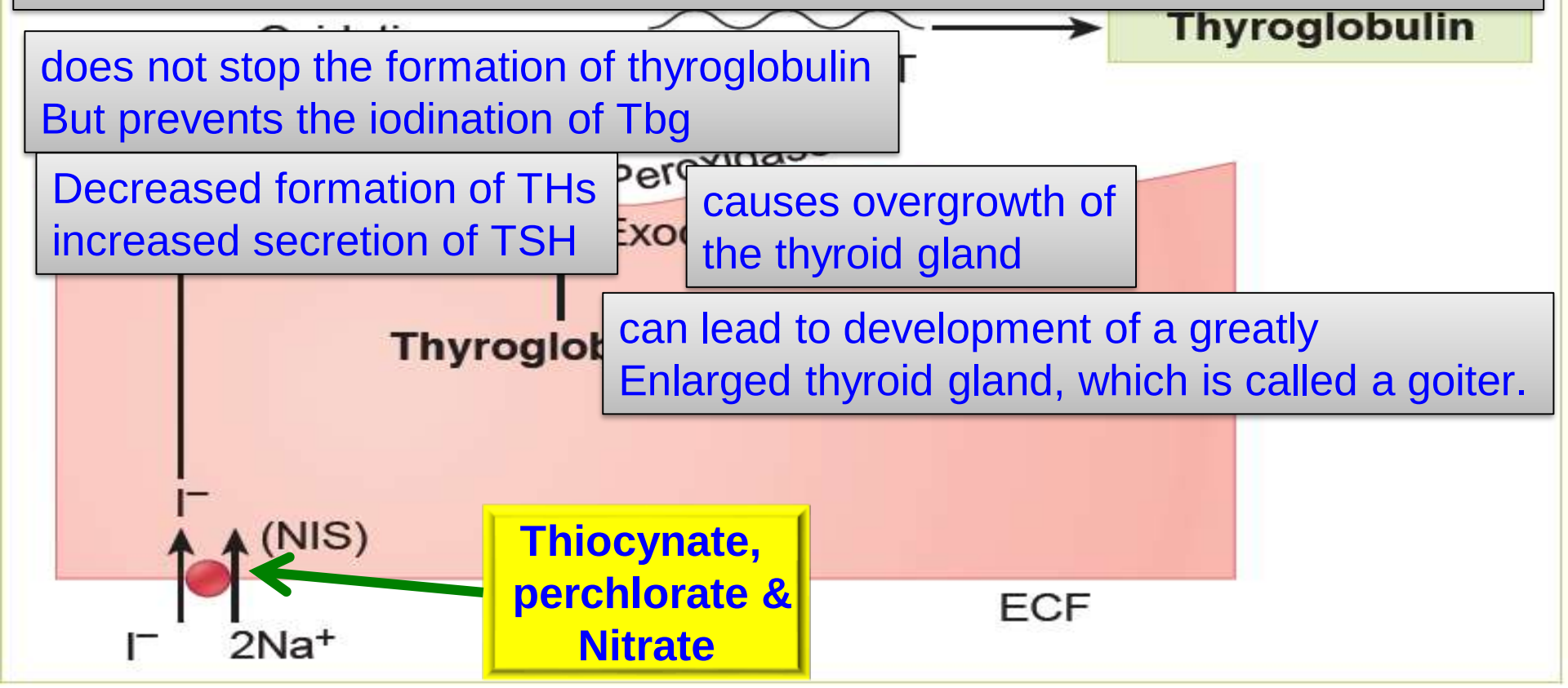
Control of thyroid hormone synthesis and secretion



Clinicals; Anti-thyroid drugs

The same active pump that transports iodide ions into the thyroid cells can also pump thiocyanate ions, perchlorate ions, and nitrate ions.

Therefore, the administration of thiocyanate (or one of the other ions as well) in high enough concentration can cause competitive inhibition of iodide transport into the cell— that is, inhibition of the iodide-trapping mechanism.



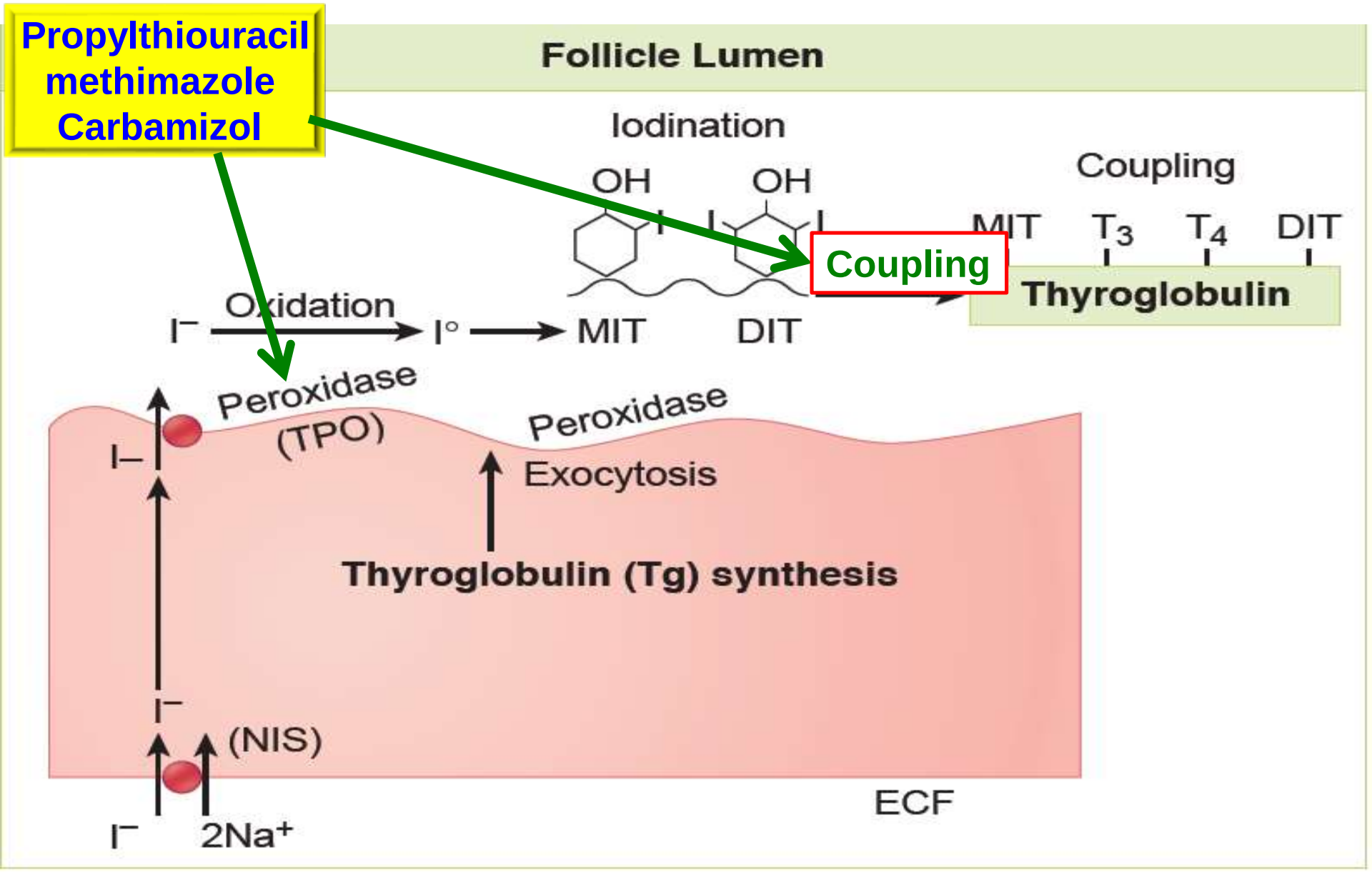
does not stop the formation of thyroglobulin
But prevents the iodination of Tbg

Decreased formation of THs
increased secretion of TSH

causes overgrowth of the thyroid gland

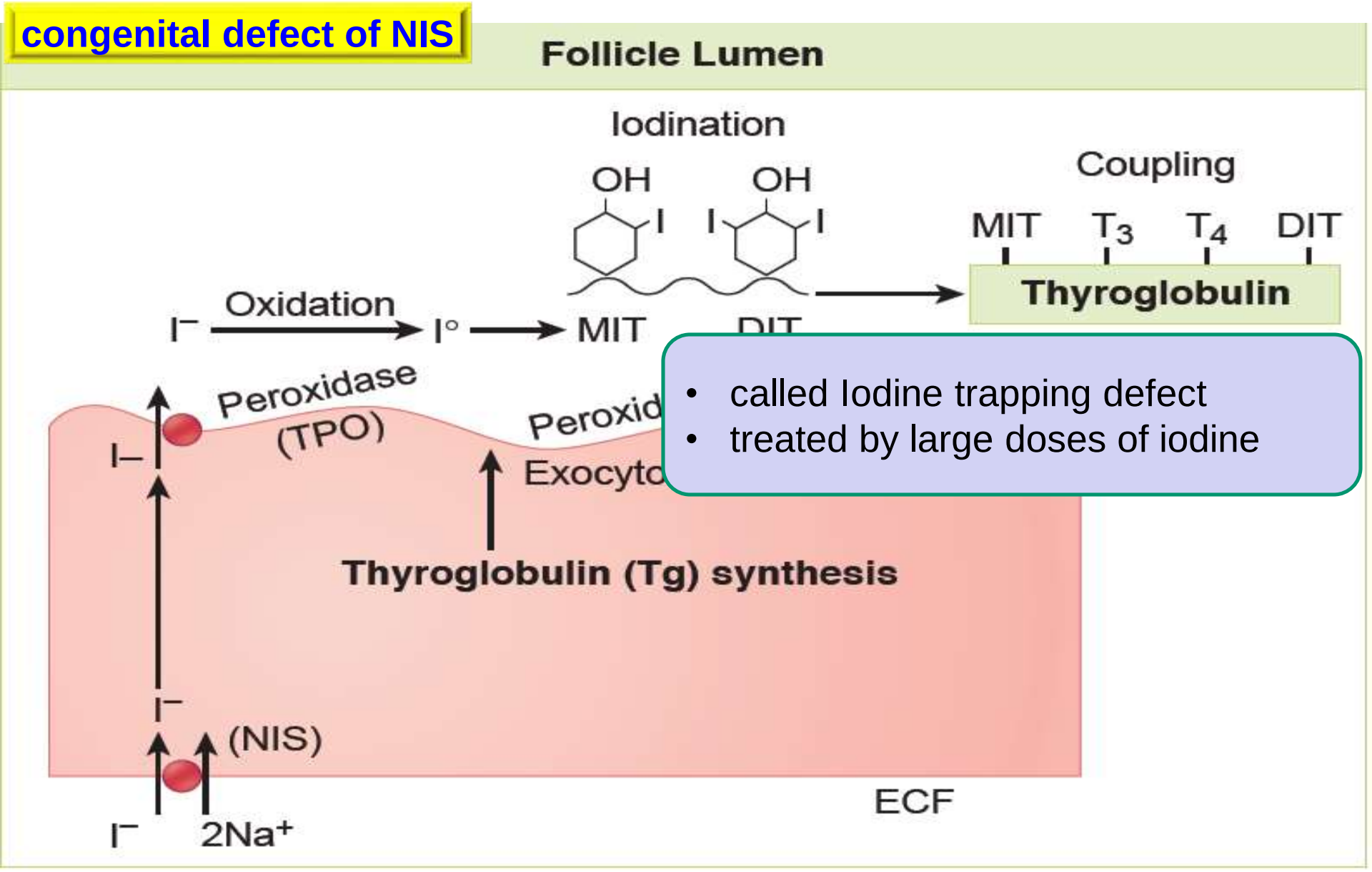
can lead to development of a greatly Enlarged thyroid gland, which is called a goiter.

Clinicals; Anti-thyroid drugs



Congenital defects

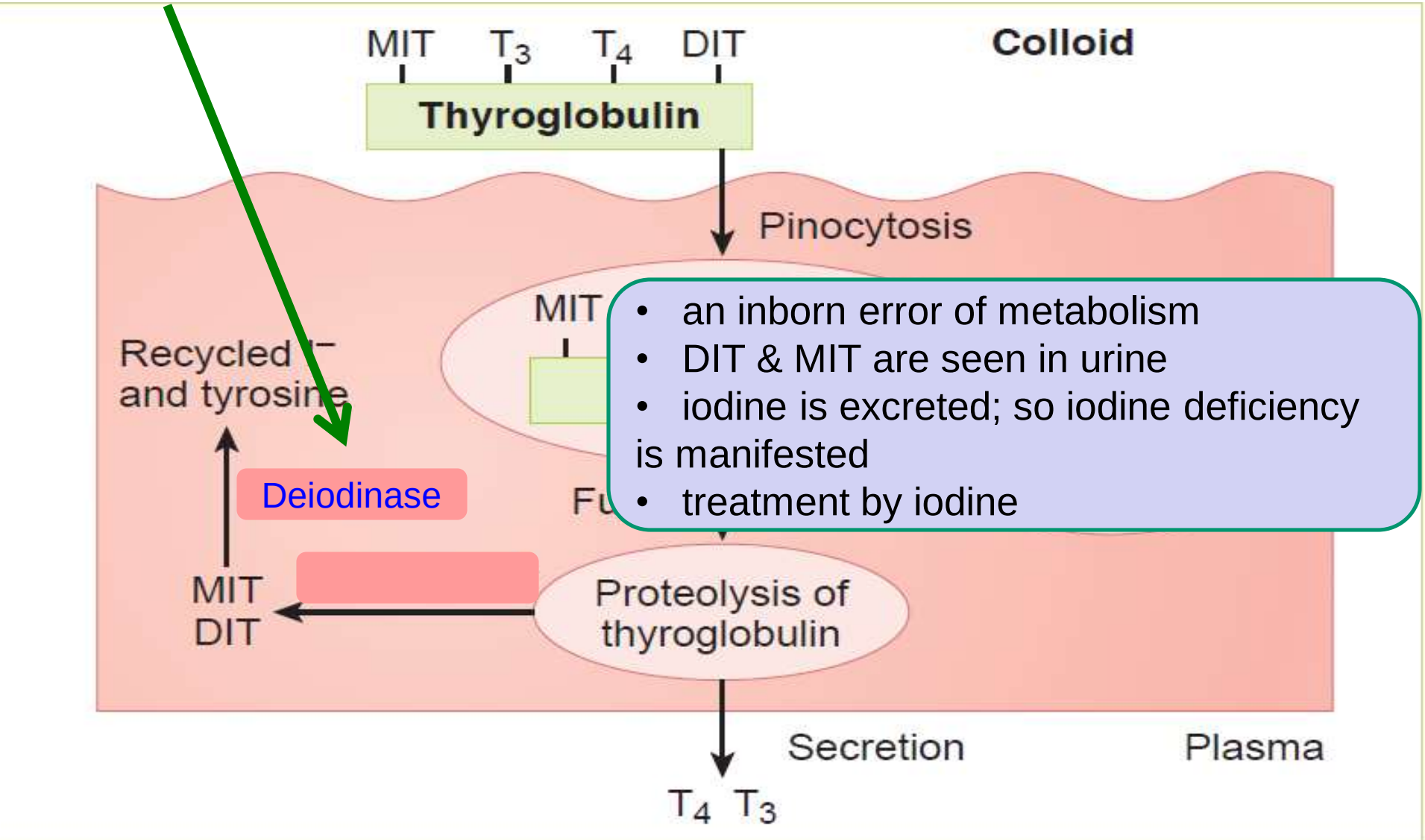
congenital defect of NIS



- called Iodine trapping defect
- treated by large doses of iodine

Congenital defects

Deiodinase defect

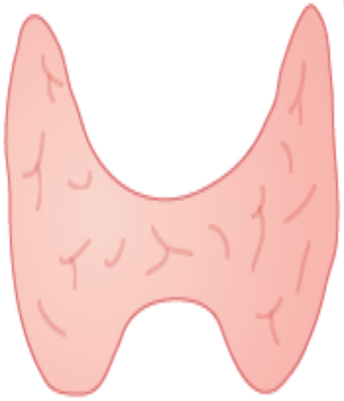


- an inborn error of metabolism
- DIT & MIT are seen in urine
- iodine is excreted; so iodine deficiency is manifested
- treatment by iodine

Thyroidal Response to Iodine deficiency

Thyrotrophs use plasma T_4 as their source for intracellular T_3, thus intracellular T_3 decreases. This allows TSH secretion to increase.

1. When iodine intake is deficient, the thyroid gland makes more T_3 and less T_4.



Thyroid gland

4. The increased TSH increases iodide trapping, and to the extent that iodine is available, maintains T_3 secretion. TSH also causes thyroid hypertrophy and goiter.

3. Increased TSH

2. Plasma T_4 is decreased.

Anterior pituitary gland

Plasma T_3 remains normal and is adequate to peripheral target tissues (liver, kidney, heart).

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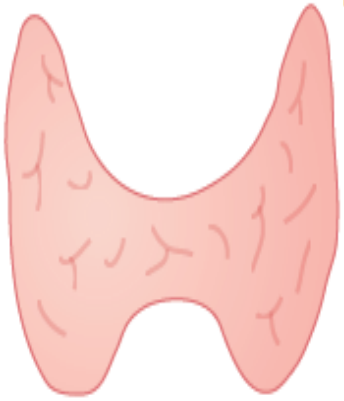

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Anterior pituitary gland

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Thyroidal Response to Excess Iodine

1. **When iodine intake is in excess the thyroid gland makes more T4 and less T3**

Thyroid gland

2. Plasma T4 is increased

Anterior pituitary gland

3. Decreased TSH

4. The decreased TSH decreases Pinocytosis as well as iodination; so both the synthesis and release of T3 & T4 will decrease TSH. Also the tonic effect of TSH is released and there will be no hyperplasia

Pathologic changes in thyroid hormone secretion

	T4	TSH	TRH
Primary hypothyroidism			
Pituitary hypothyroidism (secondary)			
Pituitary hyperthyroidism (secondary)			
Graves' disease (autoimmune)			