

DRUGS USED IN HYPOTHYROIDISM

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Learning objectives

By the end of this lecture, students should be able to:

- describe different classes of drugs used in hypothyroidism and their mechanism of action
- understand their pharmacological effects, clinical uses and adverse effects.
- recognize treatment of special cases of hypothyroidism such as myxedema coma

Hypothyroidism

- Thyroid gland does not produce enough hormones
- may be congenital, primary or secondary
- Congenital: in children, hypothyroidism leads to delay in growth (**dwarfism**), and intellectual development (**cretinism**)
- People who are most at risk include those over age 50 & mainly in females
- Prevalence is **14**/1000 females and **1**/1000 males
- Diagnosed by low plasma levels of T3 & T4 and TSH

Primary hypothyroidism

Inadequate function of the gland itself - causes

- Iodine deficiency is the most common cause of primary hypothyroidism and endemic goiter worldwide
- Autoimmune: Hashimoto's thyroiditis
- Radioactive iodine treatment of hyperthyroidism
- Post thyroidectomy
- Anti-thyroid drugs (CMZ , PTU)
- Other drugs (lithium, amiodarone)
- Sub-acute thyroiditis
- Thyroid carcinoma

Secondary hypothyroidism-causes

- Hypothalamic disease
- Pituitary disease

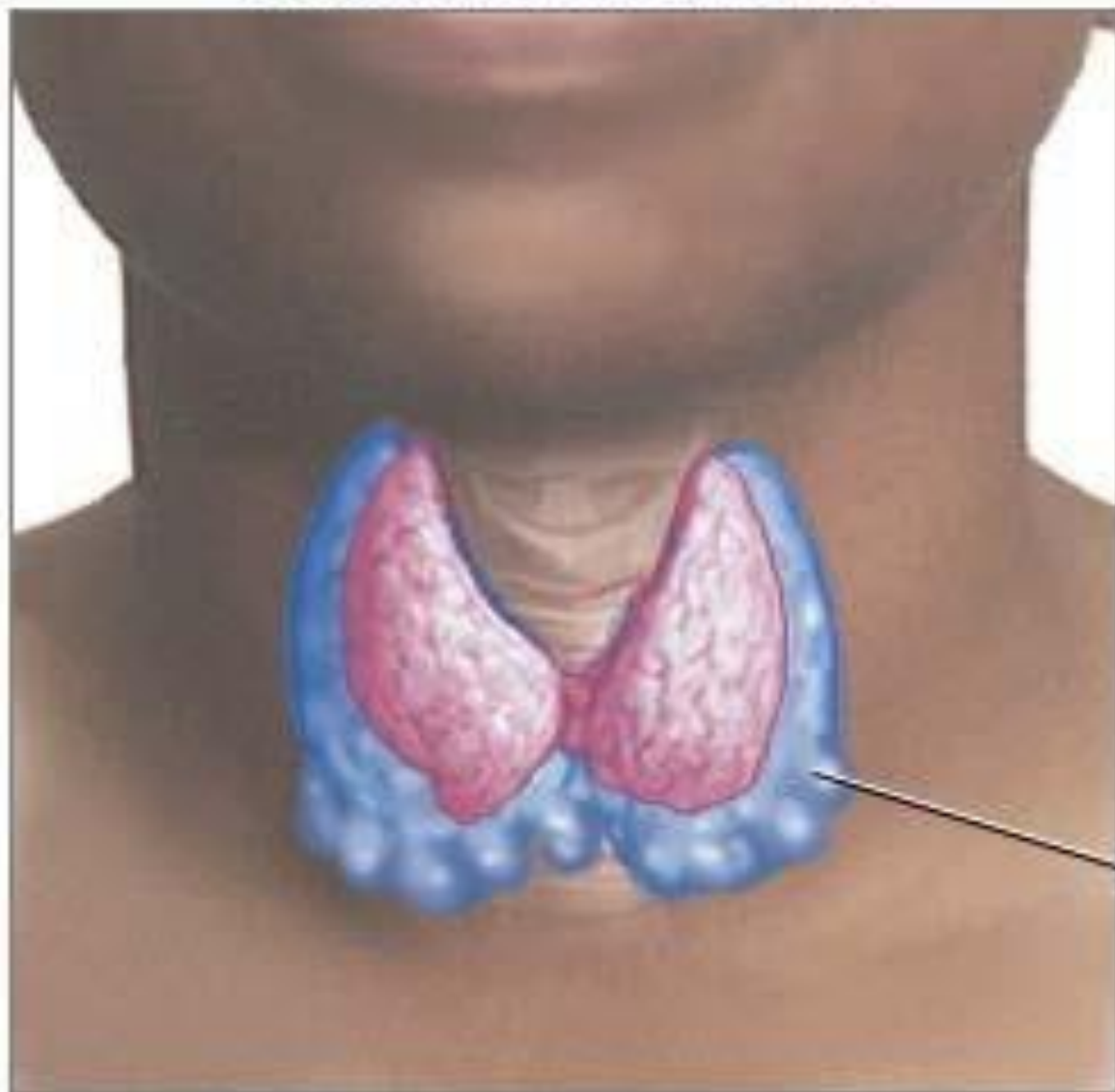
Early Manifestations of Hypothyroidism

- Fatigue and lack of energy
- Cold intolerance
- Constipation
- Weakness
- Muscle or joint pain
- Paleness
- Thin, brittle hair and fingernails

Late Manifestations of Hypothyroidism

- Decreased sense of taste and smell
- Dry flaky skin
- Hoarseness
- Menstrual disorders
- Puffy face, hands, and feet
- Thinning of eyebrows

Hashimoto's disease



Enlarged, inflamed
hypofunctioning
thyroid (goiter)







Treatment of Hypothyroidism

- **Replacement therapy with synthetic thyroid hormone preparations :**
 - **LEVOTHYROXINE (T₄)**
 - **LIOTHYRONINE (T₃)**
 - **LIOTRIX**

Thyroid preparations

- **LEVOTHYROXINE: (T_4)**
- A synthetic form of the thyroxine (T_4) , is the drug of choice for replacement therapy
- Stable and has a long half life (7 days)
- Administered once daily.
- Restore normal thyroid levels within 2-3 weeks
- Absorption is increased when hormone is given on empty stomach

Thyroid preparations

- **LEVOTHYROXINE: (T₄)**
- Oral preparations available from 0.025 to 0.3 mg tablets
- Parenteral preparation 200-500µg
- In **old patients** and in patients with **cardiac** problems , treatment is started with reduced dosage.
- Levothyroxine is given in a dose of 12.5 – 25 µg/day for two weeks and then increased every two weeks.

Clinical uses

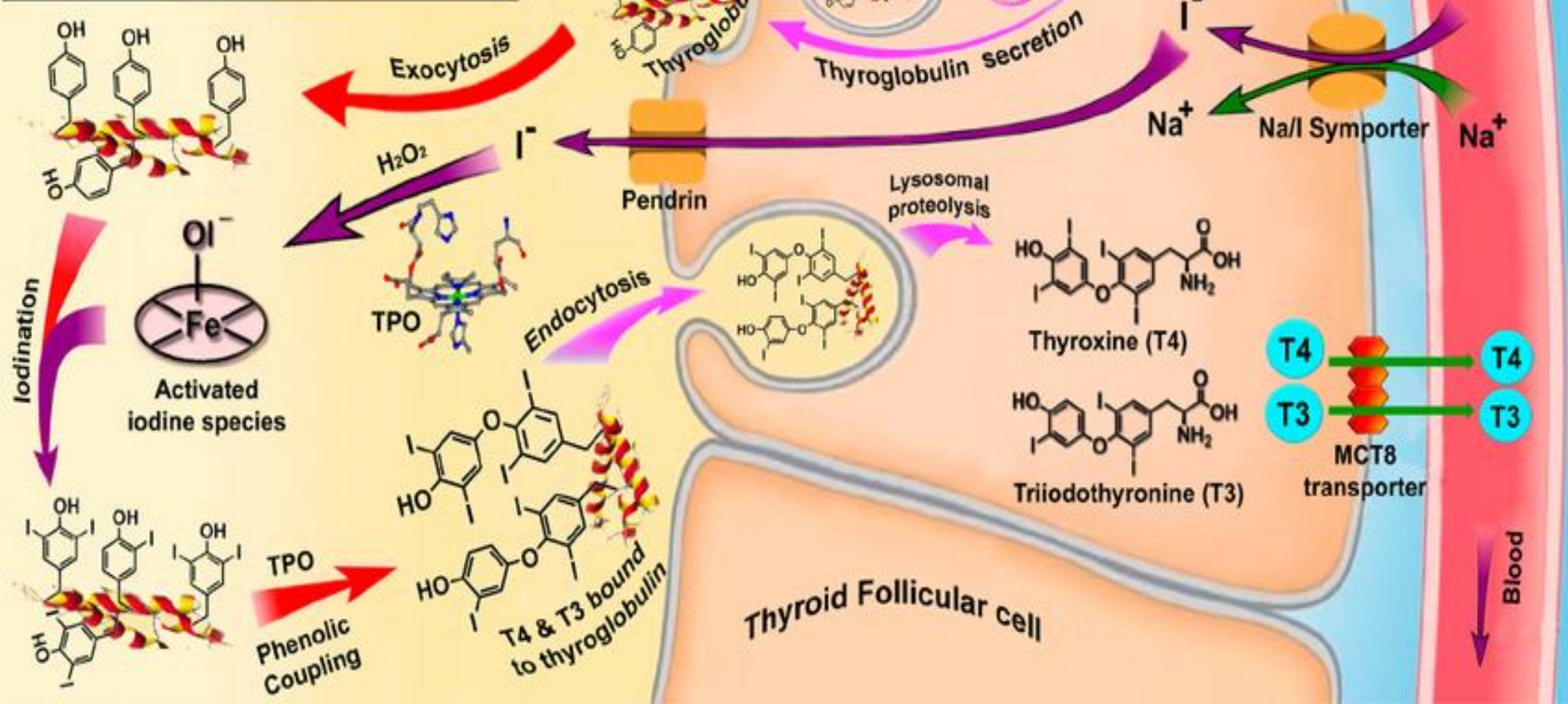
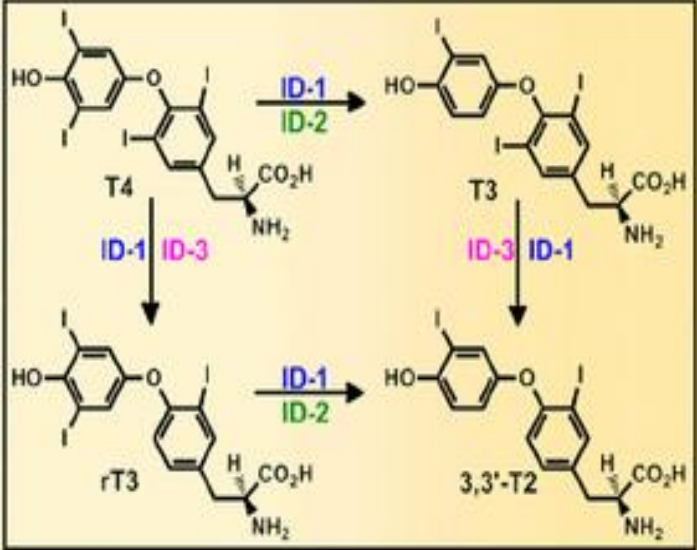
- Hypothyroidism, regardless of etiology

including :

- ❖ Congenital
- ❖ Hashimoto thyroiditis
- ❖ Pregnancy

Metabolism of thyroid hormones

- Major pathway of thyroid hormone metabolism is through sequential deiodination
- 80% of circulating T_3 is derived from peripheral T_4 by monodeiodination
- The liver is the major site of degradation for both T_4 and T_3
- 80% of the daily dose of T_4 is deiodinated to yield equal amounts of T_3 and rT_3 (reverse T_3 , which is inactive)



ADVERSE EFFECTS OF OVER DOSE

- CHILDREN :

- restlessness , insomnia
- accelerated bone maturation

- ADULTS :

- cardiac arrhythmias (Tachycardia, atrial fib.)
- tremor , restlessness ,headache
- heat intolerance
- muscle pain
- change in appetite, weight loss

Thyroid preparations

- **LIOTHYRONINE (T₃) :**
 - More potent (3-4 times) and rapid onset of action than levothyroxine
 - has a short half life - not recommended for routine replacement therapy (requires multiple daily doses)
 - should be avoided in cardiac patients
 - oral preparation available are 5-50µg tablets
 - parenteral use 10µg/ml

Pharmacokinetic of Thyroid Hormones

Hormone	Biologic Potency	$t_{1/2}$(days)	Protein Binding (%)
Levothyroxine (T₄)	1	6-7	99.96
Liothyronine (T₃)	4	≤ 2	99.5

Thyroid preparations

- **LIOTRIX :**
- Combination of synthetic T4 & T3 in a ratio 4:1 that attempt to mimic the natural hormonal secretion
- The major limitations to this product are high cost and lack of therapeutic rationale because 35% of T4 is peripherally converted to T3

MYXEDEMA COMA

- Life –threatening hypothyroidism
- The treatment of choice is loading dose of levothyroxine intravenously 300-400µg initially followed by 50µg daily.
- I.V. liothyronine for rapid response but it may provoke cardiotoxicity
- I.V. hydrocortisone may be used in case of adrenal and pituitary insufficiency.

HYPOTHYROIDISM AND PREGNANCY

- In pregnant hypothyroid patient 20-30 % increase in thyroxine is required because of :
 - elevated maternal thyroxine binding globulin (TBG) induced by estrogen
 - early development of fetal brain which depends on maternal thyroxine