

# **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

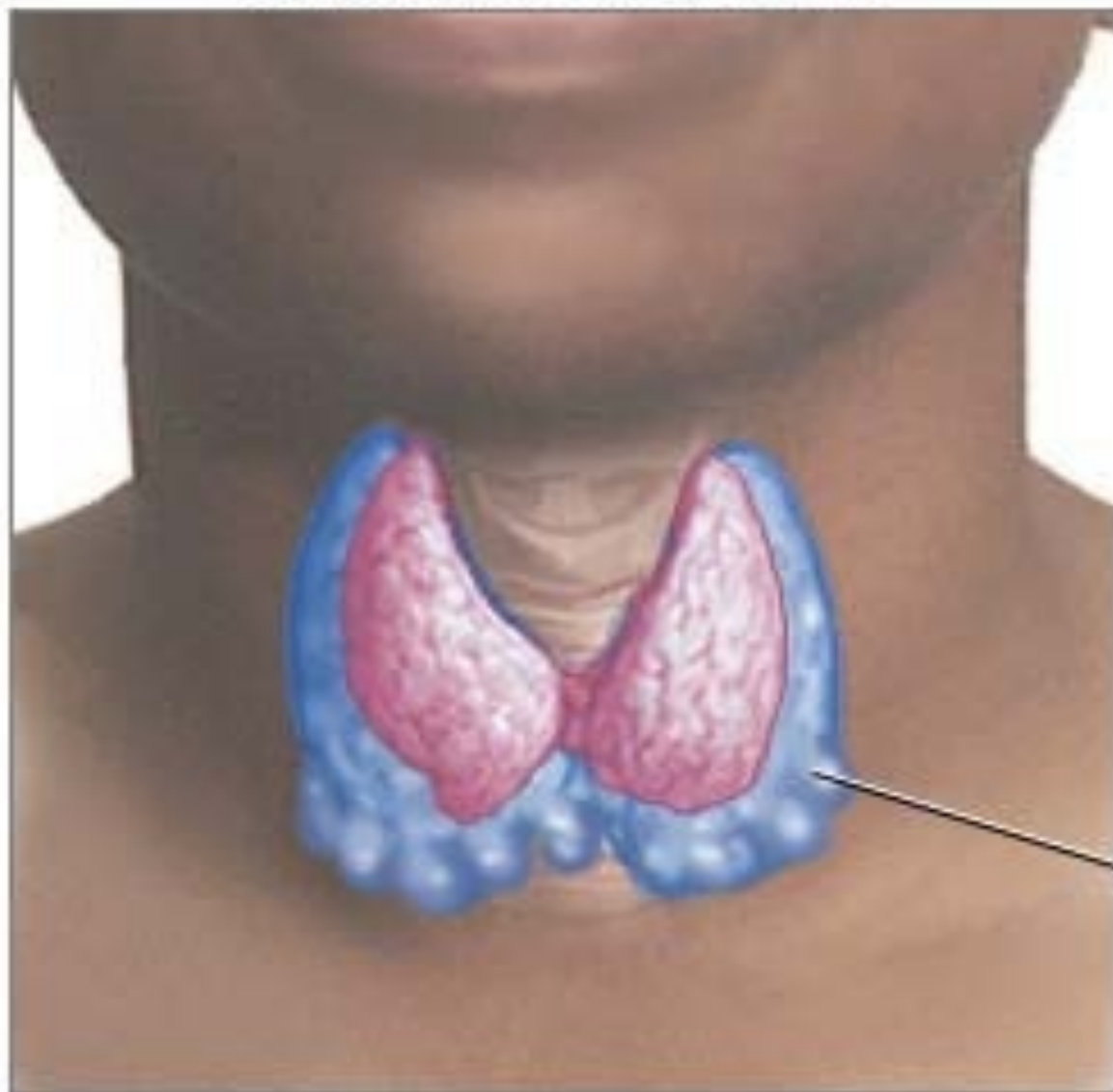
# Early Manifestations of Hypothyroidism

- 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 (T<sub>4</sub>)**
- **LIOTHYRONINE (T<sub>3</sub>)**
- **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: (T<sub>4</sub>)**
- 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

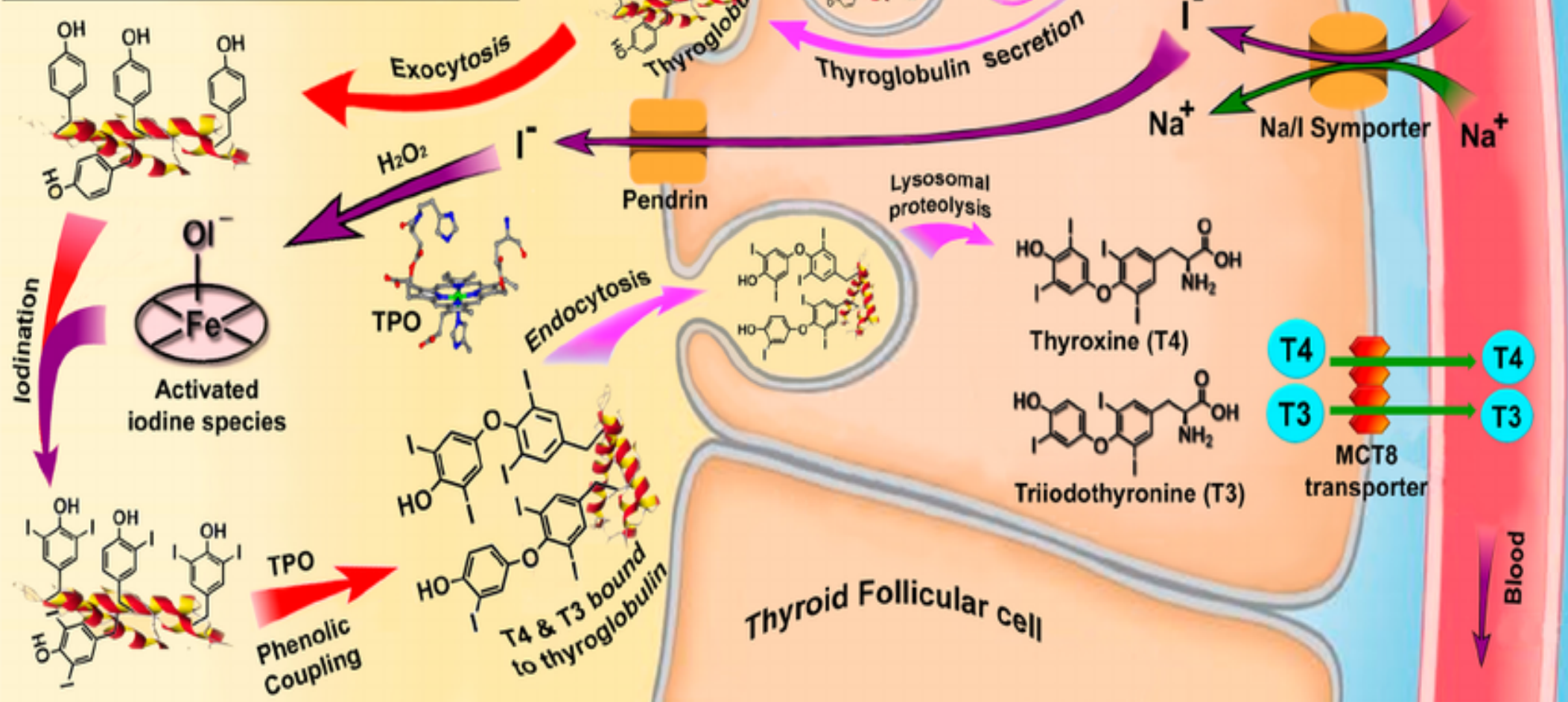
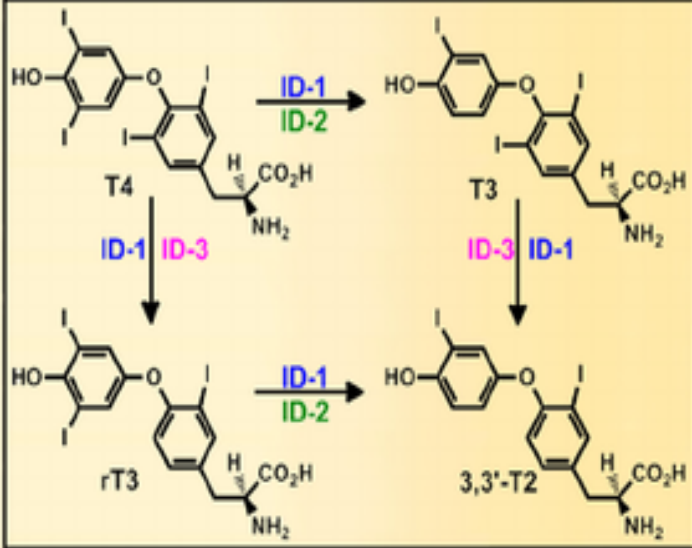
including :

- ❖ 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 (T<sub>3</sub>) :**
  - 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

<b>Hormone</b>	<b>Biologic Potency</b>	<b><math>t_{1/2}</math>(days)</b>	<b>Protein Binding (%)</b>
<b>Levothyroxine (T<sub>4</sub>)</b>	<b>1</b>	<b>6-7</b>	<b>99.96</b>
<b>Liothyronine (T<sub>3</sub>)</b>	<b>4</b>	<b>≤ 2</b>	<b>99.5</b>

# 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