



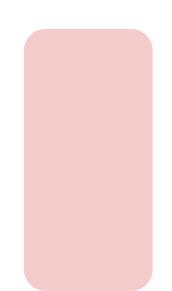


## Hypothyroidism

#### **Learning Objectives:**

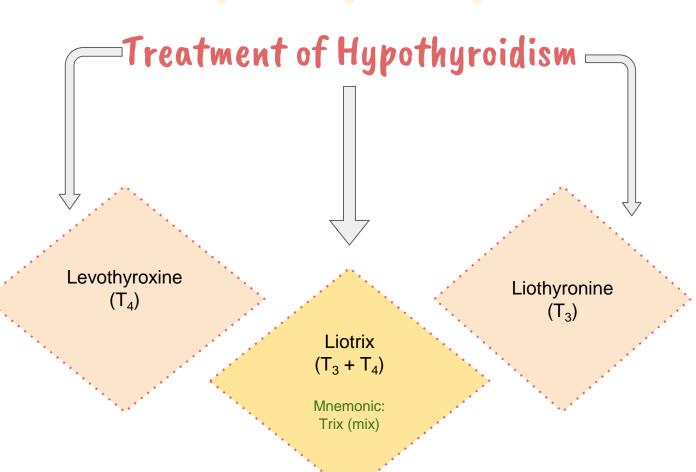
- 1- Describe different classes of drugs used in hypothyroidism and their mechanism of action.
- 2-Understand their pharmacological effects clinical uses and adverse effects
- 3- Recognize treatment of special cases of hypothyroidism such as myxedema coma

Color index:
Important
Note
Extra





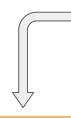






Dr. Yieldz Note: it's important to know the differences between the 3 drugs





Levothyroxine (T<sub>4</sub>)

mnemonic: LEVO (4 letters)  $\rightarrow$  T4



Liothyronine (T<sub>3</sub>)

Mnemonic: LIO(3 letters) → T3



Liotrix  $(T_3 + T_4)$ 

Mnemonic: Trix (mix)

### Hypothyroidism

### Thyroid gland does not produce enough hormones

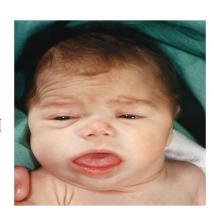
### Congenital: In children leads to:

- Delay in growth (Dwarfism)
- Delay in intellectual development (cretinism)

### primary

secondary

- 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



Pictured: Cretinism

Causes of Hypothyroidism	
Primary Hypothyroidism (inadequate function of the gland itself)	Secondary Hypothyroidism
<ul> <li>Iodine deficiency is the most common cause of hypothyroidism and endemic goiter worldwide.</li> <li>Autoimmune: Hashimoto's thyroiditis (enlarged, inflamed hypofunctioning thyroid)</li> <li>Radioactive iodine (hyperthyroidism treatment)</li> <li>Post thyroidectomy</li> <li>Antithyroid drugs (CMZ, PTU)</li> <li>Other drugs(lithium, amiodarone)</li> <li>Subacute thyroiditis</li> <li>Thyroid carcinoma</li> </ul>	<ul> <li>Impairment of higher cortical centers</li> <li>Hypothalamic disease</li> <li>Pituitary disease</li> </ul>

### **Manifestations of Hypothyroidism Early Manifestations Late Manifestations** Opposite to hyperthyroidism Decreased sense of taste and Fatigue and lack of energy smell. (Reminder: this is also an ADR Cold intolerance of methimazole, hyperthyroidism Constipation Weakness Dry flaky skin Muscle or joint pain Hoarseness **Paleness** Menstrual disorders Thin, brittle hair and Puffy face, hands, and feet fingernails(characteristic) Thinning of eyebrows

# Treatment of Hypothyroidism Replacement therapy with synthetic thyroid hormone preparations:

Drug	LEVOTHYROXINE (T4)
M.O.A	Synthetic form of thyroxine (T4), <u>drug of choice</u> for replacement therapy.
P.K	<ul> <li>Stable and has a long half life (7 days) advantage</li> <li>Administered once daily. advantage</li> <li>Restore normal thyroid levels within 2-3 weeks</li> <li>Absorption is increased when hormone is given on empty stomach</li> <li>Parenteral preparation (for emergency) and oral preparation.</li> <li>Oral preparations available from 0.025 to 0.3 mg tablets</li> <li>Levothyroxine is given in a dose of 12.5 – 25 μg/day for two weeks and then increased every two weeks.</li> <li>Major pathway of thyroid hormone metabolism is through sequential deiodination</li> </ul>
	<ul> <li>80% of circulating T3 is derived from peripheral T4 by monoiodination.</li> <li>The liver is the major site of degradation for both T4 and T3</li> <li>80% of the daily dose of T4 is deiodinated to yield equal amounts of T3 and rT3 (reverse T3 ,which is inactive)</li> </ul>
Clinical Uses	<ul> <li>Hypothyroidism, regardless of etiology including:</li> <li>Congenital</li> <li>Hashimoto thyroiditis</li> <li>Pregnancy</li> <li>Recommended for routine lifelong replacement therapy</li> </ul>
ADR Of overdose	<ul> <li>In children: restlessness, insomnia, accelerated bone maturation</li> <li>In adult: cardiac arrhythmia (tachycardia, atrial fibrillation), tremor, restlessness, headache, change in appetite, weight loss, heat intolerance, muscle pain</li> </ul>

### **Precaution:**

In old patients and in patients with cardiac problems because it causes tachycardia, treatment is started with reduced dosage.

# Treatment of Hypothyroidism Replacement therapy with synthetic thyroid hormone preparations:

Drug	LIOTHYRONINE (T3):
P.K	<ul> <li>More potent (3-4 times) and rapid onset of action than levothyroxine</li> <li>oral preparation available are 5-50μg tablets - parenteral use 10μg/ml</li> </ul>
Disadvantage + Precaution	<ul> <li>has a short half life - not recommended for routine replacement therapy (requires multiple daily doses) (T4 has a long duration of action)</li> <li>should be avoided in cardiac patients</li> </ul>
Drug	Liotrix
M.O.A	Combination of <b>synthetic T4 &amp; T3</b> in a ratio 4:1 that attempt to mimic the natural hormonal secretion
Disadvantage	The major limitations to this product are: - High cost - 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 maintenance dose
- I.V. liothyronine T3 for rapid response but it may provoke cardiotoxicity
- I.V. hydrocortisone may be used in case of adrenal and pituitary insufficiency. When there is a disturbance in the regulatory axis

### Hypothyroidism and pregnancy

In pregnant hypothyroid patient 20-30 % increase in thyroxine is required because of

- 1. elevated maternal thyroxine binding globulin (TBG) induced by estrogen
- 2. early development of fetal brain which depends on maternal thyroxine



### 1-What is the drug of choice in cases of severe hypothyroidism "myxedema coma"?

- a) I.V Liothyronine
- b) Oral Levothyroxine
- c) I.V hydrocortisone
- d) I.V Levothyroxine

### 2- which of the following drugs has a rapid onset of action but could provoke cardiotoxicity?

- a) Liotrix
- b) Levothyroxine
- c) Liothyronine
- d) Hydrocortisone.

### 3- which of the following is a limitation of Liotrix?

- A) High cost.
- B) Cardiotoxicity
- C) Multiple daily doses
- D) Hypersensitivity reactions

#### 4- which of the following is a common side effect of levothyroxine overdose?

- a) Dry skin
- b) Constipation
- c) Decreased sense of taste and smell
- d) Weight loss

### 5- all of the following statements are TRUE about levothyroxine except:

- a) Administered once daily.
- b) Best absorbed on empty stomach.
- c) Has a short half life.
- d) Restores normal thyroid function within 2-3 weeks



### Q) What is myxedema coma? And how is it managed?

Myxedema coma is a condition of life threatening hypothyroidism, it is managed by:

- 1- loading dose of levothyroxine intravenously
- 2- I.V liothyronine for rapid response.
- 3- I.V hydrocortisone in case of adrenal and pituitary insufficiency.

MCQ

2)C

3)A

5)C



### Team Leaders:

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## Thank you to those who worked on this lecture:

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### References:

✓ Doctors' slides and notes



