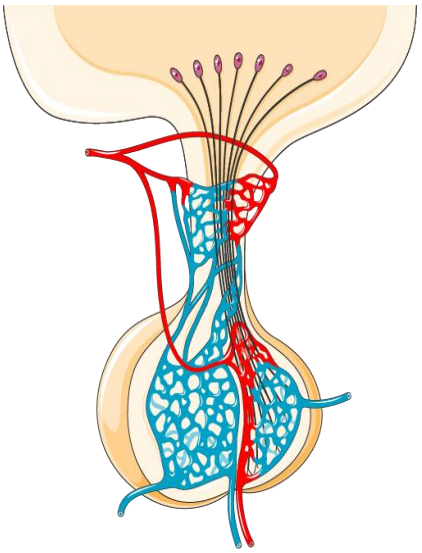
MEDICINE
KING SAUD UNIVERSITY

436 team
pharmacology



2: Drug used in hypothyroidism

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

- Extra information and further explanation
- **Important**
- **Doctors' notes**
- **Drugs names**
- **Mnemonics**

تمت المراجعة
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Kindly check the editing file before studying this document

Introduction

Hypothyroidism

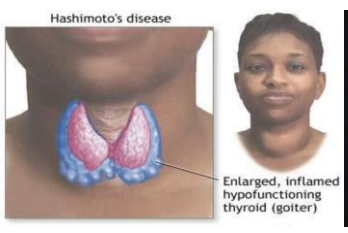
- Hypothyroidism: Thyroid gland does not produce enough hormones
- May be congenital, primary or secondary
- Congenital: in children, hypothyroidism leads to delay in growth (**dwarfism**),and intellectual development (**cretinism**)
- People who are most at risk include those over age 50 & mainly in females
- Prevalence is 14/1000 females and 1/1000 males . Common in females
- Diagnosed by low plasma levels of T_3 & T_4 and TSH

Type of hypothyroidism

Primary	Secondary
Inadequate function of the gland itself - causes : • **Iodine deficiency** is the most common cause of primary hypothyroidism and endemic goiter worldwide (hypo or hyperthyroidism could cause goiter) • **Autoimmune:** Hashimoto's thyroiditis (inflammation of the thyroid due to the presence of autoimmune antibodies which attack TSH receptors) • **Radioactive iodine treatment** of hyperthyroidism (causes destruction of the follicular cells) • Post-thyroidectomy (therapy for life) • **Anti-thyroid drugs (CMZ , PTU)** • Other drugs (lithium→ it inhibit the formation and the release of hormones , amiodarone→ it is a potent anti arithmetic drug that contains two iodine atoms , thus it stimulate the thyroid function and could cause hyper or hypothyroidism) • Sub-acute thyroiditis • Thyroid carcinoma	• **Hypothalamic disease** • **Pituitary disease**

Manifestations of Hypothyroidism

Early manifestation	Late manifestation
• Fatigue and lack of energy • **Cold intolerance** • **Constipation** • Weakness • Muscle or joint pain • Paleness • **Thin, brittle hair and fingernails**	• Decreased sense of taste and smell • Dry flaky skin • Hoarseness بحة في الصوت • Menstrual disorders • Puffy سمين face, hands, and feet • Thinning of eyebrows



Treatment of Hypothyroidism

Replacement therapy with synthetic thyroid hormone preparations :

- Levothyroxine (T_4) — Levothyroxine = 4 letters
- Liothyronine (T_3) — Liothyronine = 3 letters
- Liotrix ($T_3 + T_4$) — Liotrix = mix

المحاضرة شرحتها لنا بروف. يلدز، اللي ركزت عليه حطيناه لكم **بالعنابي**

Levothyroxine (T_4) (most common)

The lovely one

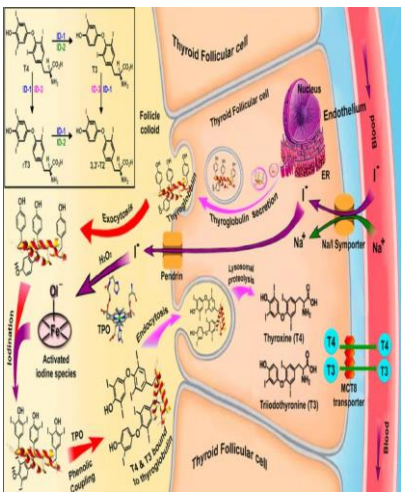
Pharmacokinetics

- A synthetic form of the thyroxine (T_4) , is the drug of choice for replacement therapy, **especially long-life thereby**, why?
  - ✓ Stable and has a long half life (7 days)
  - ✓ Administered once daily.
  - ✓ Restore normal thyroid levels within **2-3** weeks (takes time to give a therapeutic effect)
- Absorption is increased when hormone is given on **empty** stomach
- Oral preparations available from 0.025 to 0.3 mg tablets غير مهم
- Parenteral preparation 200-500µg
- Levothyroxine is given in a dose of 12.5 – 25 µg/day for two weeks and then increased every two weeks. غير مهم

M.O.A

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 هنا يقصد إن معظم تي٣ اللي بالدم تكون من تحويل تي٤ إلى تي٣ –عن طريق إزالة ذرة يود من تي٤-، أنزين ليش؟ لأن تي٤ أصلًا كميته بالجسم أكثر
- The **live**r 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) هنا يتكلم عن الهرمون اللي نعطيه أحنا (الدوا) عكس النقطة اللي قبل كان يتكلم عن الهرمون اللي يطلعه الجسم



Clinical use

Hypothyroidism, regardless of etiology including :

- Congenital
- Hashimoto thyroiditis
- Pregnancy

Treatment of Hypothyroidism

Levothyroxine (T_4) (most common)

Caution

- In old patients and in patients with cardiac problems (because it could cause tachycardia), treatment is started with reduced dosage.

(we have to take care in old patients because;
1- they don't have the same clearance as a young individual
2- they my suffer from other diseases that requires the intake of other drugs thus we take caution it to avoid drug-drug interactions)
we start with the lowest dose for two weeks and increase gradually every two weeks while checking for the hormone levels.

ADRs

OVER DOSE the symptoms which will result are similar to hyperthyroidism's symptoms

- In children: restlessness , insomnia , accelerated bone maturation
- In adult: cardiac arrhythmia (tachycardia , atrial fib), tremor , restlessness ,headache , change in appetite, weight loss , heat intolerance , muscle pain thus it is advisable to check for the thyroid hormones levels continuously
- Less side effects then T_3, why? Basically bc T_3 more active than T_4 ⟶ more effect on the body

Liothyronine (T_3)

Potent and rapid like a **lion** !

Pharmacokinetics

- More potent (3-4 times) and rapid onset of action than levothyroxine (advantage)
- It has **short half life**, so not recommended for routine replacement therapy (requires multiple daily doses) and because it's potent it should be avoided in cardiac penitents
- Oral preparation available are 5-50µg tablets
- Parenteral use 10µg/ml

C.I

should be avoided in cardiac patients, why? As you know from physiology T_3 has very strong effect on CVS -↑ heart function-, and cardiac patients already have ↑ heart function يعني أكيد بتسوء حالتهم

Let's say, **Cardiac patient** may have cardiac arrest when they see a **lion** !

Pharmacokinetic of Thyroid Hormones

Hormone	Biologic Potency	$T_{½}$ (days)	Protein Binding (%)
Levothyroxine (T_4)	1	6-7	99.96%
Liothyronine (T_3)	4	≤ 2	99.5%

Treatment of Hypothyroidism

Liotrix	
M.O.A	Combination of synthetic **T_4 & T_3 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 T_4 is peripherally converted to T_3

Myxedema coma

- Life –threatening hypothyroidism
- The treatment of choice is loading dose (high dose) of levothyroxine intravenously 300-400µg initially followed by 50µg daily. الجرعات غير مهمه
- **I.V.** liothyronine for rapid response but it may provoke cardiotoxicity (we have to test heart function before to not risk his life)
- **I.V.** hydrocortisone may be used in case of adrenal and pituitary insufficiency.
- After this we give a symptomatic treatment

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

Summary

	LEVOTHYROXINE (T4)	LIOTHYRONINE (T3)	LIOTRIX
Indication	• A synthetic form of the thyroxine (T4) , 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 • Oral preparations available from 0.025 to 0.3 mg tablets • Parenteral preparation 200-500µg • Levothyroxine is given in a dose of 12.5 – 25 µg/day for two weeks and then increased every two weeks.	• More potent (3-4 times) and rapid onset of action than levothyroxine • as a short half life ; not recommended for routine replacement therapy (requires multiple daily doses) • oral preparation available are 5-50µg tablets • parenteral use 10µg/ml 19	
M.O.A	**Metabolism of thyroid hormones :** • Major pathway of thyroid hormone metabolism is through sequential deiodination • 80% of circulating T3 is derived from peripheral T4 by monodeiodination • The liver is the major site of degradation for both T4 and T3 • 80% of the daily dose of T4 is deiodinated to yield equal amounts of T3 and rT3 (reverse T3 ,which is inactive)		Combination of synthetic T4 & T3 in a ratio 4:1 that attempt to mimic the natural hormonal secretion
Clinical use	Hypothyroidism, regardless of etiology including : • Congenital • Hashimoto thyroiditis • Pregnancy		
C.I	In old patients and in patients with cardiac problems , treatment is started with reduced dosage.	should be avoided in cardiac patients	The major limitations to this product are high cost and lack of therapeutic rationale because 35% of T4 is peripherally converted to T3
ADRs	**OVER DOSE** • In children: restlessness , insomnia , accelerated bone maturation • In adult : cardiac arrhythmia (tachycardia , atrial fib.), .) tremor , restlessness ,headache , change in appetite, weight loss , heat intolerance , muscle pain		

MCQs

Q1: A 42 years old female came to the clinic and complain of weakness & fatigue and lack of energy and weight gain. Also she mentioned that she has cold intolerance and her hairs started to be brittle. The physician request the thyroid function test and the result shows there is markedly decreased in the level of both T3 & T4. Which drug of the following is the drug of choice in her case for long life thereby ?

A- Liothyronine. *B- Levothyroxine.* *C- Liotrix.*

Q2: Which drug can be used in emergency case due to its rapid of onset and its potent effect ?

A- Liothyronine. *B- Levothyroxine.* *C- Liotrix.*

Q3:Which drugs of the following is highly contraindicated in patient with cardiac disease due to its cardiotoxicity ?

A- Liothyronine. *B- Levothyroxine.* *C- Liotrix.*

Q4: Which drugs of the following is acting by mimicking the natural hormonal secretion of thyroid gland?

A- Liothyronine. *B- Levothyroxine.* *C- Liotrix.*

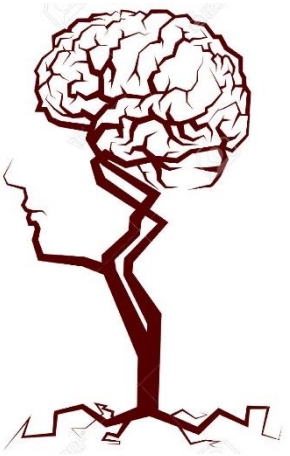
Q5: Why is it essential to increase the dose up to 30% in women with hypothyroidism during pregnancy ?

A- The elevated estrogen induced the thyroxine binding globulin.
B- The maternal thyroxine is essential for development of fetal brain.
C- Both of them.

Q6: 56 years old Patient who is diagnosed with hypothyroidism with weight gain, cold intolerance, fatigue and lack of energy and brittle nails. The doctor perscribed 0.46 mg tablets of drug as treatment. Three day later, his symptoms completely changed to the opposite. He develop tremor, heat intolerance, weight loss and clubbing of the fingers. What is the underlying cause behind this condition?

A- he develops Iodism and overdose of iodine.
B- he develops secondary hyperthyroidism.
C- he develops overdose of levothyroxine.

1. B
2. A
3. A
4. C
5. C
6. C



إِنَّ فِي ذَٰلِكَ لَآيَاتٍ لِّقَوْمٍ يَتَفَكَّرُونَ ﴿٣﴾

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