



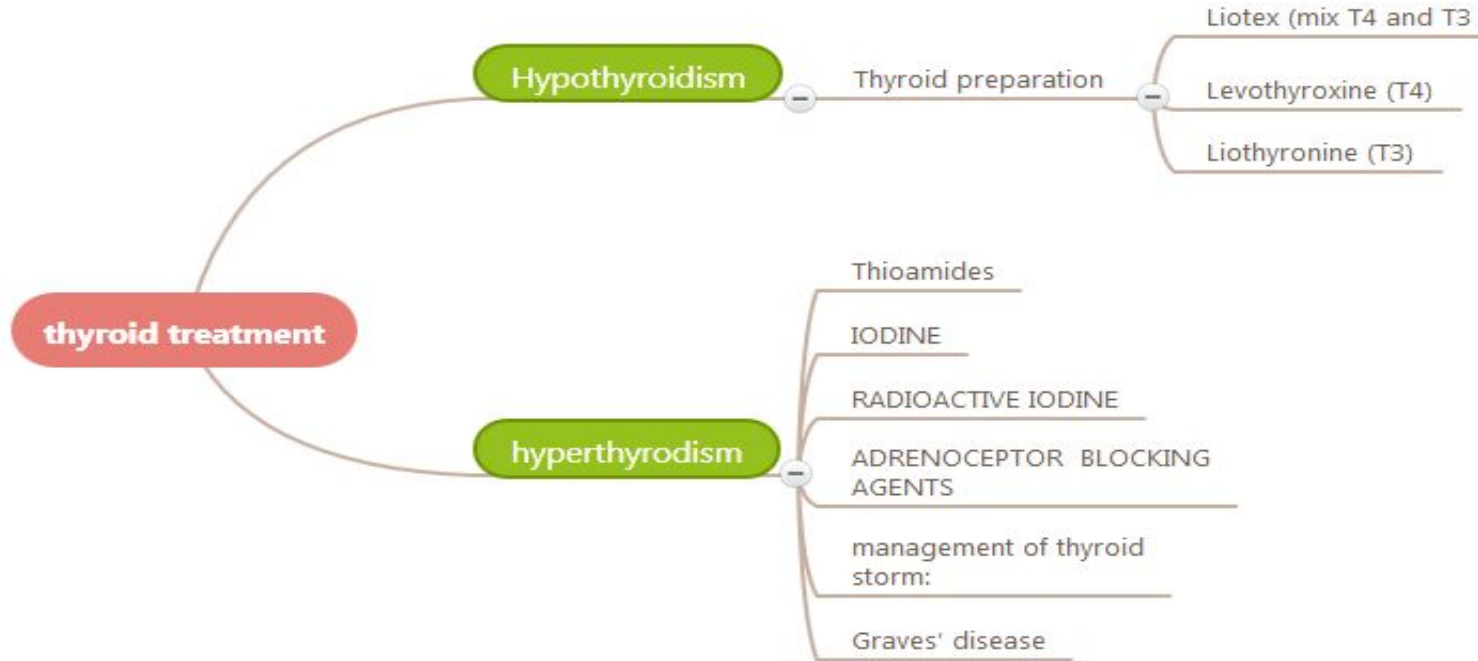
# Lecture 1 & 2

## Drugs used in hyperthyroidism and hypothyroidism

### Objectives:

- ★ **Describe** different classes of drugs used in hyperthyroidism and hypothyroidism and their mechanism of action
  - ★ **Understand** their pharmacological effects, clinical uses and adverse effects
  - ★ **Recognize** treatment of special cases such as during pregnancy, Graves' disease , thyroid storm, Myxedema coma
- Additional Notes
  - **Important**
  - Explanation –Extra-

# mind map



before starting, please check our [endocrine block correction](#)

# Introduction:

## Thyroid Hormones Disorders

\*The Doctor said that they will not ask about physiology part, it is just for more understanding of the Pharmacological Action → We just mention The most Important Part of it..

Thyrotoxicosis	Hyperthyroidism	Hypothyroidism	Thyroid neoplasm
<p>Is the term for all disorders with increased levels of circulating thyroid hormones</p> <p>Hypermetabolic state caused by thyroid hormone excess at the tissue level</p>	<p>Refers to disorders in which the thyroid gland secretes increased amounts of hormones</p> <p>Increased thyroid hormones synthesis and secretion</p>	<p>Refers to disorders in which the thyroid gland secretes decreased amounts of hormones</p>	<p>Benign enlargement or malignancies of the gland</p>

### Causes of thyrotoxicosis:

#### With high RAIU

#### With low RAIU

- Graves' disease (60-80%)
- Multinodular goitre (14%)
- Adenomas / carcinomas

- Thyroiditis
- Iodine-induced thyrotoxicosis drugs (e.g. amiodarone)
- radiographic contrast media



\*note : All patients with hyperthyroidism have thyrotoxicosis but Not all patients with thyrotoxicosis have hyperthyroidism

# Hyperthyroidism

## features of Graves Disease (Diffuse Toxic Goiter)

Caused by thyroid stimulating immunoglobulins that stimulate TSH receptor, resulting in sustained thyroid over activity

- Mainly in young adults aged 20 to 50
- 5 times more frequent in women
- Swelling and soft tissues of hands and feet
- Clubbing of fingers and toes
- Half of cases have Exophthalmos (not seen with other causes of hyperthyroidism)
- 5% have pretibial myxedema (thyroid dermopathy)

## Features of Toxic Multinodular Goiter

- Second most common cause of hyperthyroidism
- Most cases in women in 5th to 7th decades
- Often have long standing goiter
- Symptoms usually develop slowly

## THYROTOXICOSIS

### Symptoms

- irritability
- Dysphoria
- Heat intolerance & sweating
- palpitation
- fatigue&weakness
- Weight loss
- Diaerrhea

### Signs

- Arrhythmias
- Thyroid enlargement
- Warm, moist skin
- Exophthalmus
- Pretibial myxedema



## Treatment of Hyperthyroidism

- **Thioamides** (*antithyroid drugs*)
- Iodides
- Radioactive iodine
- Beta blockers
- **THYROIDECTOMY** • Sub-total thyroidectomy is the treatment of choice in very large gland or multinodular goiter

# Thioamides

Drugs	Propylthiouracil ( PTU )	Methimazole & Carbimazole ( carbimazole is prodrug converted to the active metabolite methimazole)
MOA	-Inhibit synthesis of thyroid hormones by inhibiting the <b>peroxidase</b> enzyme that catalyzes the iodination of tyrosine residues	
	Propylthiouracil ( <b>but</b> not methimazole ) blocks the conversion of T4 to T3 in peripheral tissues	
Pharmacokinetics	<ul style="list-style-type: none"><li>-Rapidly absorbed</li><li>-<b>80-90% protein binding</b></li><li>-accumulate in thyroid</li><li>-<b>excrete in kidney as inactive metabolite within 24h.</b></li><li>-short duration of action (1.5hrs half life)</li><li>-administration every 6-8 hrs</li><li>-crosses placenta <b>* Recommended in pregnancy (Crossing placenta is less readily as it is highly protein bound )</b></li><li>-Less secreted in breast milk <b>*Recommended in breast feeding</b></li></ul>	<ul style="list-style-type: none"><li>-Rapidly absorbed</li><li>-<b>most of the drug is free</b></li><li>-accumulate in thyroid</li><li>-<b>Excretion slow, 60-70% of drug is recovered in urine in 48 hrs</b></li><li>-long duration of action (6hrs half life)</li><li>--administration every 8 hrs</li><li>-Concentrated in Thyroid &amp; crosses placenta Not recommended in pregnancy <b>(C.I)</b></li><li>-secreted in breast milk <b>*not recommended (C.I)</b></li></ul>

# Thioamides

Drugs	Propylthiouracil ( PTU ) & Methimazole	propylthiouracil	methimazole
ADV	<ul style="list-style-type: none"><li>● <b>Skin reactions</b></li><li>● <b>Arthralgia</b></li><li>● <b>Polyarthrits</b></li><li>● <b>GIT effects</b></li></ul> <p>sharing the same ADV</p>	<ul style="list-style-type: none"><li>● Immunoallergic hepatitis</li><li>● ANCA-positive vasculitis <i>(Anti-neutrophil cytoplasmic antibodies)</i></li></ul>	Abnormal sense of taste or smell
	★ <b>Agranulocytosis:</b> Seen in patients with Graves' disease; occurs within 90 days of treatment		

# IODINE (Lugol's solution, potassium iodide)

## Examples

- Organic iodides as : iopanoic acid or ipodate
- Potassium iodide

## Mechanism of action

- Inhibit thyroid hormone synthesis and release
- Block the peripheral conversion of T4 to T3
- The effect is not sustained ( produce a temporary remission of symptoms )

## Therapeutic uses

- Prior to thyroid surgery to decrease vascularity & size of the gland
- Following radio-active iodine therapy
- Thyrotoxicosis

## Precautions / toxicity

- Should not be used as a single therapy
- Should not be used in pregnancy**
- May produce iodism ( Rare, as iodine is not much used now)

- **Iodism Symptoms:**  
skin rash , hypersalivation  
oral ulcers bad breath.

# RADIOACTIVE IODINE ( RAI )

## MOA

Accumulates in the thyroid gland and destroys parenchymal cells, producing a long-term decrease in thyroid hormone levels.

## Pharmacokinetic

- Clinical improvement may take 2-3 months
- Half-life 5 days
- Cross placenta & excreted in breast milk
- Easy to administer ,effective , painless and less expensive
- Available as a solution or in capsules

## clinical uses

- Hyperthyroidism mainly in old patients (above 40)
- Graves' disease
- Patients with toxic nodular goiter
- As a diagnostic

## Disadvantages

- High incidence of delayed hypothyroidism
- Large doses have cytotoxic actions ( necrosis of the follicular cells followed by fibrosis )
- May cause genetic damage
- May cause leukemia & neoplasia



# ADRENOCEPTOR BLOCKING AGENTS

<b>Mechanism of action</b>	Adjunctive therapy to relieve the adrenergic symptoms of hyperthyroidism such as tremor, palpitation, heat intolerance and nervousness.
<b>Examples</b>	Propranolol, Atenolol , Metoprolol
<b>contraindication</b>	Propranolol is contraindicated in asthmatic patients

## Thyrotoxicosis during pregnancy:

Better to start therapy before pregnancy with  $^{131}\text{I}$  or subtotal thyroidectomy to avoid acute exacerbation during pregnancy



During pregnancy radioiodine is contraindicated, Propylthiouracil is the drug of choice during pregnancy.



## Thyroid storm:



- A sudden acute exacerbation of all of the symptoms of thyrotoxicosis, presenting as a life threatening syndrome.
- There is hyper metabolism, and excessive adrenergic activity, death may occur due to heart failure and shock.
- It is a medical emergency .



## management of thyroid storm:

- should be treated in an ICU for close monitoring of vital signs and for access to invasive monitoring and inotropic support
- Correct electrolyte abnormalities, Treat cardiac arrhythmia ( if present ) & Aggressively control hyperthermia by applying ice packs
- Promptly administer antiadrenergic drugs (e.g. propranolol) to minimize sympathomimetic symptoms
- High-dose Propylthiouracil (PTU) is preferred because of its early onset of action ( **risk of severe liver injury and acute liver failure** )
- Administer iodine compounds (Lugol's iodine or potassium iodide) orally or via a nasogastric tube
- Hydrocortisone 50 mg IV every 6 hours to prevent shock.
- Rarely, plasmapheresis has been used to treat thyroid storm

# Management of Hyperthyroidism due to Graves' disease

## Severe Hyperthyroidism



[ markedly elevated serum T4 or T3  
very large goiter, > 4 times normal ]



Definitive therapy with radioiodine preferred in  
**adults**



Normalization of thyroid function with anti-thyroid  
drugs before surgery in **elderly patients** and those  
with heart disease

## Mild/moderate hyperthyroidism



[ small or moderately enlarged thyroid; children or pregnant or lactating women ]



Primary anti-thyroid drug therapy  
should be considered



Start methimazole, 5–30 mg/day,  
**(PTU preferred in pregnant women)**



Monitor thyroid function every 4–6 wk  
until **euthyroid state** achieved



**Discontinue** drug therapy after 12–18 mo



**Monitor** thyroid function every 2 mo for 6 mo then less frequently



**Relapse**



**Remission**

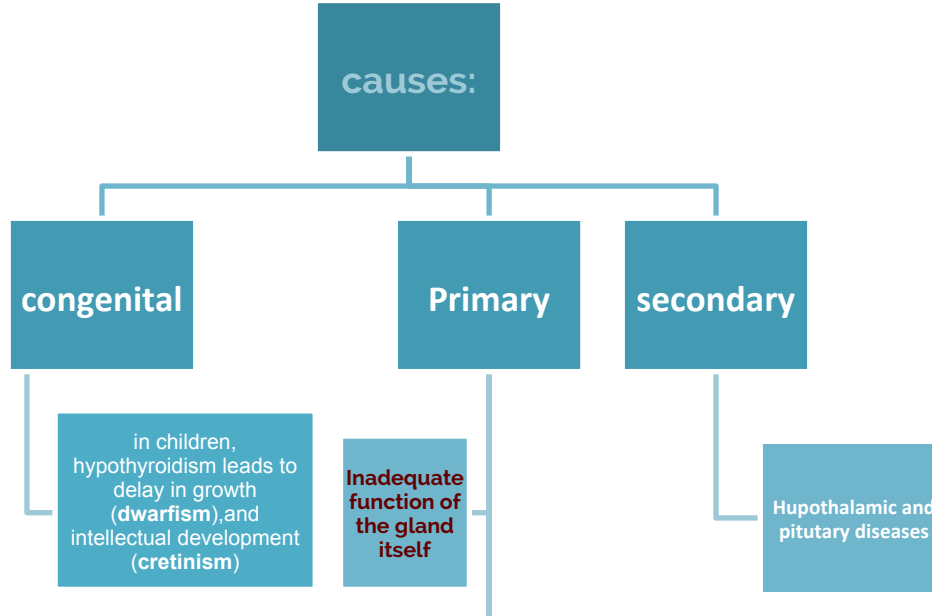
Definitive radioiodine  
therapy in adults  
**(Second course of anti-thyroid  
drug therapy in children)**

Monitor thyroid function  
every 12 mo indefinitely

# Hypothyroidism

**definition:** Thyroid gland does not produce enough hormones

- affect People who are most at risk include those over **age 50** & mainly in **females**
- Diagnosed by low plasma levels of T3 & T4 and TSH



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, amioderone)

Sub-acute thyroiditis

Thyroid carcinoma

# manifestation of hypothyroidism

## early manifestation

Fatigue and lack of energy

Constipation

Cold intolerance

Muscle or joint pain

Paleness

Thin, brittle hair and fingernails

Paleness

## late manifestation

Decreased sense of taste and smell

Dry flaky skin

Hoarseness

Menstrual disorders

Puffy face, hands, and feet

Thinning of eyebrows

# treatment of hypothyroidism: Thyroid preparation

	Levothyroxine (T4)	Liothyronine (T3)	Liotex (mix T4 and T3)
Pharmacokinetics	<ul style="list-style-type: none"><li>● A synthetic form of the thyroxine (T4) , is the drug of choice for replacement therapy.</li><li>● Stable and has a long half life ( 7 days).</li><li>● Administered once daily.</li><li>● Restores normal thyroid levels within 2-3 weeks.</li><li>● <b>Absorption is increased when hormone is given on empty stomach.</b><ul style="list-style-type: none"><li>● Oral preparations available from 0.025 to 0.3 mg tablets.</li><li>● Parnteral preparation 200-500μ.</li></ul></li><li>★ in old patient and patient with any cardiac problems, start with reduced (12.5 – 25 μg/day) for two weeks and then increased every two weeks.</li></ul>	<ul style="list-style-type: none"><li>● More potent (3-4 times) and rapid action than levothyroxine .</li><li>● has a short half life, not recommended for routine replacement therapy (because it's given multiple daily doses).</li><li>● oral preparation available.</li><li>● parenteral use. (used in life threatening cases)</li></ul>	<ul style="list-style-type: none"><li>● Combination of synthetic T4 &amp; T3 in a ratio 4:1 that attempt to mimic the natural hormonal secretion .</li><li>● The major limitations of this product are <b>high cost</b> and <b>lack of therapeutic rationale</b> because 35% of T4 is peripherally converted to T3, so the drug is under the study yet.</li></ul>

	Levothyroxine (T4)	Liothyronine (T3)	Liotex (mix T4 and T3)
Clinical use	<p><b>Any Hypothyroidism case</b> ,regardless of etiology ( including Congenital ,Hashimoto thyroiditis , Pregnancy and Thyroid carcinoma ) .</p>	-	-
ADR	<p><b>Overdose in children:-</b> restlessness , insomnia and accelerated bone maturation</p> <p><b>Over dose in adult :-</b></p> <ul style="list-style-type: none"> <li>-cardiac arrhythmias (Tachycardia, atrial fib.) -</li> <li>tremor , restlessness ,headache</li> <li>-heat intolerance</li> <li>-muscle pain</li> <li>-change in appetite, weight loss</li> </ul>	<p><b>Should be avoided in cardiac patient</b></p>	-

## 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 in pregnancy:

- ★ In pregnant hypothyroid patient, very important that the dose must be increased **20-30 %** more than the normal dose of non-pregnant women.

### because of :

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



# MCQs

**1/A patient has hyperthyroidism after treating him he developed vasculitis (ANCA+) which one of these drugs is most likely to have side affect :**

- A-PTU
- B-Mithmazole
- C-Liotrex
- D-Levothyroxine

**2/a 30-yaer old patient who has severe hyperthyroidism . to manage his case we should star treat him with :**

- A-mithemazol
- B-Beta blockers
- C-PTU
- D-radioiodine

**3/a 5-year old patient was diagnosed with mild hyperthyroidism which of the these drugs should we start with :**

- A-PTU
- B-Mithemazole
- C-Radioactive iodine
- D-Propranolol

**4/patient who developed thyrotoxicosis he was treated with drug that caused to him hypersalivation,oral ulceration and metallic taste which of these drugs can cause such side affect :**

- A-aspirin
- B-potassium iodide
- C-mithemazol
- D-liotrex

**5/a patient that was treated with hyperthyroidism then after few months he developed few side affect such as agranulocytosis and abnormal sense smell . which one of the following drugs can lead to such side affects :**

- A-Radioactive iodine
- B-Anti-thyroid
- C-Iodides
- D-beta blockers

# MCQs

**6/ A cardiac patient was diagnosed with hypothyroidism, which drug we should avoid :**

- A-Levothyroxine
- B-Liotrix
- C-Liothyronine

**7/Liotrix is a:**

- A-Combination of synthetic T4 & T3
- B-(T3)
- C-synthetic form of the thyroxine(T4)

**8/ A child with hypothyroidism his mother noticed that he is recently become growing fast and can't sleep at night what is the drug :**

- A-Liotrix
- B-Liothyronine
- C-Levothyroxine

**9/ a 83 year cardiac patient was diagnosed with hypothyroidism what to do if you'll prescribe**

**(Levothyroxine):**

- A. Reduce the dose
- B. Increase the dose
- C. It is contraindicated

**10/ A patient with Myxedema Coma was diagnosed to have adrenal and pituitary insufficiency the treatment is :**

- A-Liotrix
- B- I.V. hydrocortisone
- C- I.V.levothyroxine

**Answers: 1.A 2.D 3.B 4.B 5.B 6.C 7.A 8.C 9.A 10.B**

# Good luck!

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