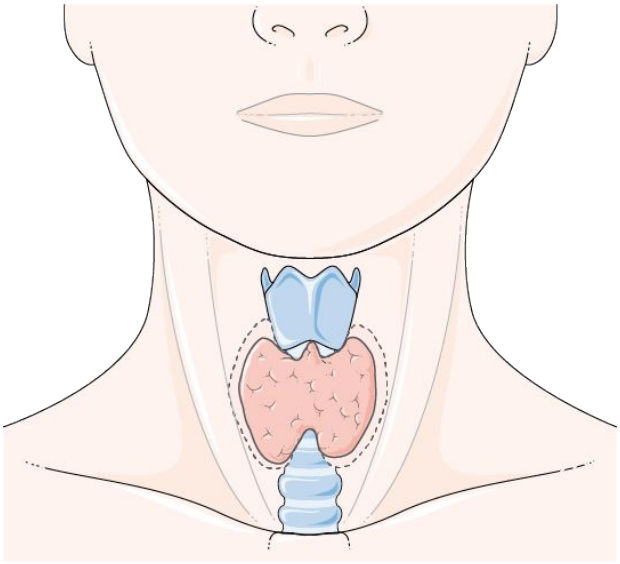
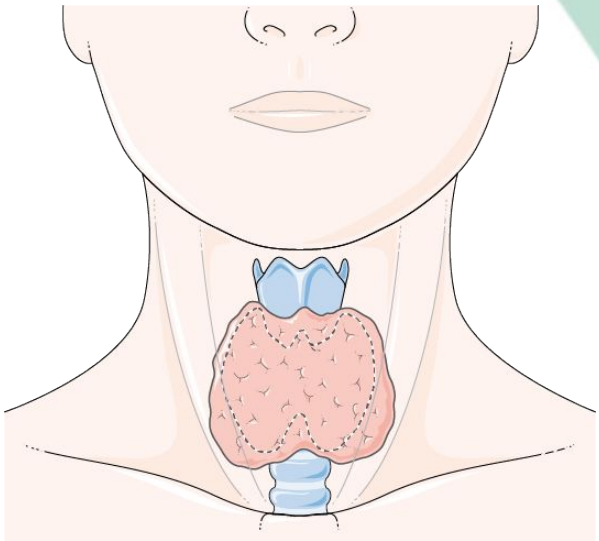
6+7





Physiology & Disorders of Thyroid Gland

Editing File

ENDO Physiology

Color Index :

- Main Text
- Important
- Girls Slides
- Boys Slides
- Notes
- Extra

Objectives

Lecture 1

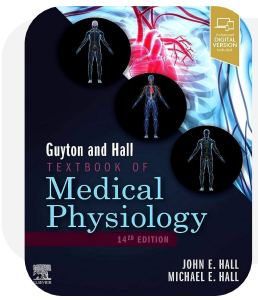
- LIST THYROID GLAND HORMONES
- DESCRIBE THE SYNTHESIS OF THE THYROID HORMONES
- DESCRIBE THE RELEASE AND ACTIONS OF THYROID HORMONES
- DESCRIBE THE NEGATIVE FEEDBACK MECHANISM (CONTROL)
- Diagram the control over the thyroid gland.
- Compare between the hormones released by the thyroid gland.

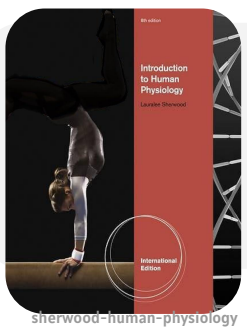
Lecture 2

- Identify the terms goiter, hypo & hyperthyroidism.
- List the causes & types of goiter, hypo & hyperthyroidism.
- Discusses the clinical picture of hypo & hyperthyroidism.
- Explain the laboratory tests to diagnose hypo & hyperthyroidism.
- Outline management regimen for hypo & hyperthyroidism.
- DESCRIBE PATHOPHYSIOLOGY BEHIND THE CAUSES OF HYPER-HYPOTHYROIDISM.
- DESCRIBE PATHOPHYSIOLOGY BEHIND THE SIGNS AND SYMPTOMS OF HYPER-HYPOTHYROIDISM.
- List The Treatment

Resources

Only ENDO chapters included





sherwood-human-physiology

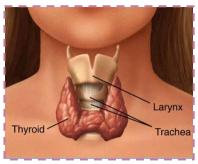
Osmosis 8min:

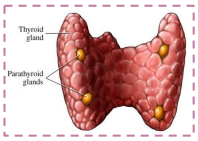
This lecture was presented by:
Dr. Nervana Mostafa - Prof. Abdulmajeed Aldrees

Thyroid gland

Introduction

- It is located below the larynx on either sides and anterior to the trachea.
- The first recognized endocrine gland
- 20g in Adults
- Thyroid gland is made of follicles.
- It's highly vascularized.
- Follicles are lined by follicular cells.
- The surrounded pinkish material is colloid.
- 2 lobes connected by isthmus in front of the trachea
- (not attach to it, only sliding over it).





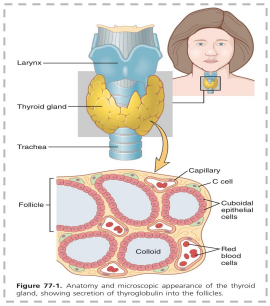


Figure 77-1. Anatomy and microscopic appearance of the thyroid gland, showing secretion of thyroglobulin into the follicles.

Three Unique features of thyroid gland

1 Contains a large amount of iodine
- supplied in diet.
- Img/week

2 Synthesis is partially intracellular and partially extracellular

3 T4 is the major product(1)
T3 the most active form

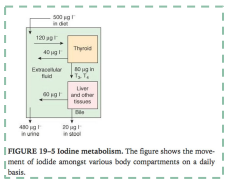
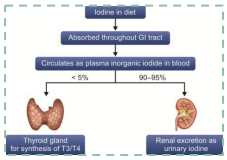
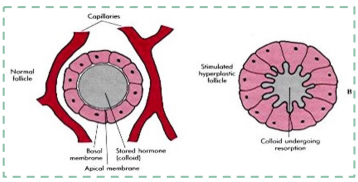
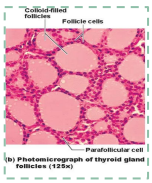


FIGURE 19–5 Iodine metabolism. The figure shows the movement of iodide amongst various body compartments on a daily basis.



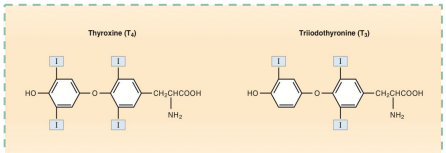
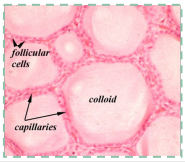
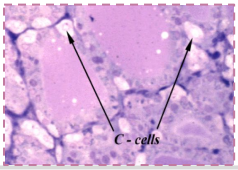
Hormones and synthesis





Thyroid gland hormones

الكمية عكس الاكتفتي يعني كلما زادت الكمية قل نشاط الهرمون (أقلهم كمية أكثر هم نشاط)

Hormones	T3 (Triiodothyronine) *Contains 3 iodine* Most potent	T4 Thyroxine (Tetraiodothyronine) *Contains 4 iodine* When it reaches the tissue its majority will be converted to T3	Calcitonin Hormone ↓ Ca++ blood levels (Humoral stimulation) (For Ca^{++} metabolism)	Reverse T3 Biologically inactive, but it appears in chemical reactions
Amount	10% Less but has stronger action than T4	90%	-	-
Site of synthesis	Apical and basal membrane in follicular cells		Parafollicular cells C -cell	-
Site of stores	In colloid			-
Structure	 			Mirrored image of T3 having 3 Iod, but the problem is the mispositioning of iod, making it inactive.

(1)Why is that a unique feature?
Because usually the most potent hormone should be secreted more which is T3, but here T4 is the major product even though it's less potent than T3.

Please check Page 17 for better understanding of the steps أضغطني

Biosynthesis of thyroid hormone

Female slides

Steps of Biosynthesis of thyroid hormones (T3-T4) by follicular cells:

1. **Iodide pump.**
2. **Thyroglobulin synthesis.**
3. **Oxidation of iodide to iodine.**
4. **Iodination** of tyrosine, to form mono-iodotyrosine (MIT) & di-iodotyrosine (DIT)
5. **Coupling:** MIT + DIT = Tri-iodothyronine, (T3). DIT + DIT = Tetra-iodothyronine, (T4)/Thyroxine.
6. **Release.**

1- Thyroglobulin Formation and Transport

Thyroglobulin is a protein. For it to be formed, we'll start with the absorption of amino acids from the circulation. 442
Tyrosine is the building block of thyroglobulin.
Thyroglobulin is formed of 140 **Tyrosine** (Main amino acid + Glycoprotein)
It is formed in **Rough endoplasmic reticulum & Golgi apparatus**

2- Iodide Pump or Iodide Trap

Active transport (Which is sodium iodide cotransporter) (against its conc. gradient, because iodine inside the follicular cell is higher).
Wolff-chaikoff effect : a reduction in thyroid hormone levels caused by administration of a large amount of iodine(I)
Ratio of concentration from **30-250 times** (In gland compared to blood).
It is stimulated by TSH (The pump number & activity will be increased in response to TSH from anterior pituitary gland, also stimulate all the steps of thyroid hormones synthesis).

3- Oxidation of Iodide To Iodine

Catalyzed by **Thyroid Peroxidase**. (Thyroid Peroxidase = converts iodide to iodine (oxidation) so it can bind to thyroglobulin).
It is located in or attached to the apical membrane of their follicular cell (Intracellular).

4- Organification of Thyroglobulin AKA: Iodination

- Binding iodine with Thyroglobulin. Where ? in the colloid
- Catalyzed by **Thyroid Peroxidase** to form MIT & DIT.
- Remain attached to thyroglobulin until the gland stimulated to secret.

5- Coupling Reaction

- **DIT + DIT = T4 (faster),**
- **while DIT + MIT = T3**
- DIT = 2 Iod molecules, MIT = 1 Iod molecule. So MIT + DIT = 3 (T3) and DIT + DIT = 4 (T4)
- Catalyzed by **Thyroid Peroxidase.**
- **It is stored as colloid.**
- Is sufficient for **2-3 months** (That's why hypo/hyperthyroidism symptoms will appear late)

عندنا **follicular cell** و في النص الهرمون **as a colloid** و إذا احتجته أسوي **endocytosis** هل ينفع يطلع للدم؟ لا، اكسره و أطلع **T3** و **T4**.

6- Endocytosis of Thyroglobulin

- When the thyroid gland is stimulated, iodinated thyroglobulin (with its attached T4 T3, MIT, and DIT) is endocytosed from the colloid into the follicular epithelial cells.
- T4 and T3 are stored in colloid > when we need them > pinocytosis.

بالمختصر.. تنوكل من ال **colloid** وتدخل مرة ثانية بال **follicular cell** عشان تروح الدم

7- Fusion of Lysosomes Immediately with the Vesicles

Once it enters follicular cells lysosomes bind with the vesicles and hydrolysis occurs.
Enter follicular cells > attach to lysosome.

8- Hydrolysis of the peptide bond to release DIT+MIT+T4+T3 from the Thyroglobulin

- Hydrolysis and break down > release of T4 and T3.
- MIT + DIT: recycle to reuse and enter the process of synthesis again.

9- Delivery of T4 and T3 to the systemic circulation

- By concentration gradient → target cells → action.
- Once needed, they're released.

10-Deiodination(2) of DIT and MIT by Thyroid Deiodinase (Recycling)

Monoiodotyrosine and Diiodotyrosine > deiodinase and will be reuse or recycle.

(I)تطبيق لنظرية العرض والطلب: لما الناس تسمع عن سلعة بتخلص يركضون عشان يشترونها، نفس الشي لما يوصل اليود للدم يكون قليل، هذا بيأثر على نشاط الpump يزيده و يأخذ كل اليود الموجود و العكس صحيح.
في السابق كانوا يستخدمون هذه الطريقة لعلاج **Thyrotoxicosis.** (negative feedback)

2- Deiodination is a process of separating iodine and Tyrosine in DIT & MIT to use Tyrosine again in synthesis of Thyroglobulin & also to reuse the iodine. (Opposite of step 4)

Thyroid Hormones in The Circulation

Bound
Biologically inactive

- 70 - 80% bound to Thyroxine-Binding Globulin (TBG) synthesized in the liver.
- The remaining is bound to albumin.

T3,T4 bind with ?

Unbound (Free)
Biologically active

- Small amount
- 0.03% of T4
- 0.3% of T3 (more, because it's the needed form, Free hormone it's the only type that triggers negative Feedback and it is the active form).
- Responsible of action.

1. In Hepatic Failure / Liver disease

❖ Low TBG → High free T3/T4 in the blood → inhibition of thyroid secretion. (Thyroid enzymes will be in the low normal range) Why? Remember -v feedback?!!

2. In Pregnancy

- Estrogen stimulates the expression of TBG.
- High estrogen → High TBG → Low free T3/T4 in the blood → stimulation of thyroid secretion.
- Pregnant women feels hot due to increase T3 & T4 Why? Remember -v feedback?!! للمره المليون
- Does it mean every pregnant have hyperthyroidism? No but it means that her thyroid hormone level will be physiologically increased into the upper normal limit.

Release of T4 & T3 Into The Tissues

1A The release is a slow because of the high affinity of the plasma binding proteins

1B
- ½ of T4 in the blood is released every 6 days
- ½ of T3 in the blood is released every one day

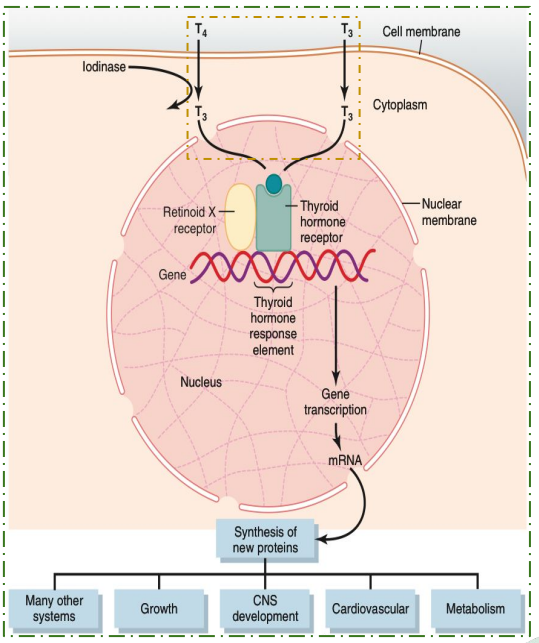
2 T3 and T4 readily diffuse through the cell membrane

3 Stored in the targeted tissues (days to weeks).

4 Most of T4 is deionized to T3 by 5-iodinase enzyme. To enter the nucleus easily يعني يرجع يتحول T3 ليه؟ لانه اقوى طيب ليه قليل ؟ ٦ ايام عشان يطلع من الدم 1B

5 In the nucleus, T3 mainly binds to "Thyroid Hormone Receptor" and influence transcription of genes*

They can cross cell membrane and nuclear membrane



Action of Thyroid Hormones

❖ Before binding to the nuclear receptors, 90% of T4 is converted to T3.

1. T3 binds to the nuclear receptor forming a T3-receptor complex
2. Activation of thyroid regulating element on the DNA
3. High DNA transcription → formation of mRNA
4. Translation of mRNA → specific protein synthesis
5. Target tissue specific

Action of thyroid hormones:

Calculate your BMR here!

1- Basal metabolic rate (BMR):

- Simply, it's the amount of energy the body needs to maintain basal functions under complete rest.
- Is the energy required under basal condition, which is the state of mental and physical rest (12-18 hours after a meal).

الخلايا لها سرعة حركة معينة ممكن تزيد وممكن تقل، عشان تستمر الحركة نحتاج طاقة، لما تقعد مريّح ١٣-١٦ ساعة بعد الوجبة الجسم بيحتاج هالمصدر من الطاقة.

- BMR is greatly influenced by the thyroid hormones Parallel increase high TH=high BMR
  - Complete lack of the thyroid hormones → ↓40-50% in BMR.
    (If there is no thyroid hormones energy amount decrease to half)
  - Extreme increase of thyroid hormones → ↑60-100% in BMR. That why weight loss
    (If there is thyroid hormone excess the amount of energy is doubled, Because it affects O2 consumption in cells).

بعد ما الجسم خلاص هضّم وتخلص من الجلوكوز BMR هو كمية الطاقة الأساسية الموجود

2- Effect on Metabolism:

Effect on carbohydrate metabolism:	Effect on fat metabolism:	Effect on protein metabolism:
ما دام هو يزيد metabolism ، فهو يحتاج glucose. - Increase glucose uptake by cells. For metabolic action - Increase glycogenolysis. - Increase gluconeogenesis. - Increase absorption from the GIT. - End result: ↑Blood glucose level	- Increase lipolysis. - Decrease plasma cholesterol by increase loss in feces. (hypothyroidism associated with atherosclerosis) - Increase oxidation of free fatty acids.	- Overall effect is catabolic leading to decrease in muscle mass. هذي المرحلة يكون الجسم اكل الجلوكوز واكل الدهون بقى العضلات

Female slides

- The metabolic effects are due to the **induction of metabolic enzymes**:
  1. Cytochrome oxidase.
  2. NADPH cytochrome C reductase.
  3. Alpha- glycerophosphate dehydrogenase.
  4. Malic enzymes.
  5. Several proteolytic enzymes.

3- Effect on the Cardiovascular system:

- Increase heart rate & stroke volume (increased contractility) which **raises or increase the Cardiac output to 60%.** → increase delivery of oxygenated blood to the tissue.
- Decrease peripheral resistance* (Peripheral vasodilation)→ increase delivery of oxygenated blood to the tissues, **arterial blood pressure doesn't increase.**
- **The end result is increased delivery of oxygenated blood to the tissues** (secondary to the first two points)
- **The cardiovascular effects are due to:**

1- Indirect:

The Thyroid hormones potentiate the effect of **catecholamine** in the circulation → activation of β-adrenergic receptors. Permissive action on catecholamines.

2- Direct induction of:

- Myocardial β-adrenergic receptors. + ive effect
- Sarcoplasmic reticulum.
- Ca+2 ATPase.
- Myosine.

Action of thyroid hormones cont...

4- Effect on the CNS

Perinatal period /Fetal and postnatal life:

- Thyroid hormones are essential for **CNS maturation.**
- So **perinatal** decrease of hormone secretion (hypothyroidism) leads to **irreversible mental retardation.**
- **Early screening is necessary to introduce hormone replacement.**
  - If it is detected in the newborn, **early hormone replacement can reverse the CNS effect** (as in sleeping a lot and inactivity, however, if it reaches the stage of retardation that is irreversible)
  - **If the baby isn't responsive, inactive, sleeps a lot → thyroid hormone deficiency.**

In adult:

- **Increased thyroid secretion:** (Hyperthyroidism = tremor)
  1- Hyperexcitability. (discussed later)
  2- Irritability. (discussed later)
- **Decreased thyroid secretion:** عكس الهايبر
  1- Slow movement. (discussed later)
  2- Impaired memory. (discussed later)
  3- Decreased mental capacity.

5- Effect on bone:

- Promote bone formation.
- Promote ossification.
- Promote fusion of bone plate.
- Promote bone maturation.

(We said promote because the action is done by growth hormone).

6- Effect on Respiration:

- Increase ventilation rate (Increased metabolism → Increased CO2 → Stimulation of respiratory centers to increase ventilation to exhale CO2)
- Increase dissociation of oxygen from hemoglobin by increasing red blood cell 2,3 DPG (2,3 diphosphoglycerate) (Direct effect on RBCs)

(2,3-DPG will decrease the affinity of the RBC & increase the loading to the tissue)

All of these aiming to deliver O_2 easily and quickly to all tissues.

7- Effect on the GIT:

- Increase <u>appetite</u> and food intake. Due to fast metabolism
- Increase <u>secretion</u> of digestive juices.
- Increase GIT <u>motility</u>:
  - Excess secretion of the hormone will lead to diarrhea → Hyperthyroidism
  - Lack of secretion of the hormone will lead to constipation → Hypothyroidism
  - <u>Hyper</u>thyroidism = <u>Increase</u> appetite and loss of weight وش قلت لك فوق ؟.
  - <u>Hypo</u>thyroidism = <u>Decrease</u> appetite and gain weight.

Increase GIT motility > diarrhea > weight loss لأنه زي ما قلنا: الاشخاص اللي يبون يخسرون وزن يأخذون thyroxine

8- Effect on Autonomic Nervous System:

- Thyroid hormone interact with the sympathetic nervous system
- Produced by the same actions of catecholamines via β-adrenergic receptors, including:

(both synergism due to similar effects and permissiveness due to potentiation of adrenergic receptors)

- Increased BMR.
- Increased heat production.
- Increased heart rate.
- Increased stroke volume

For example, **the beta-blocker** (propranolol) is used in **hyperthyroidism treatment.**

Regulation of Hormones Secretion

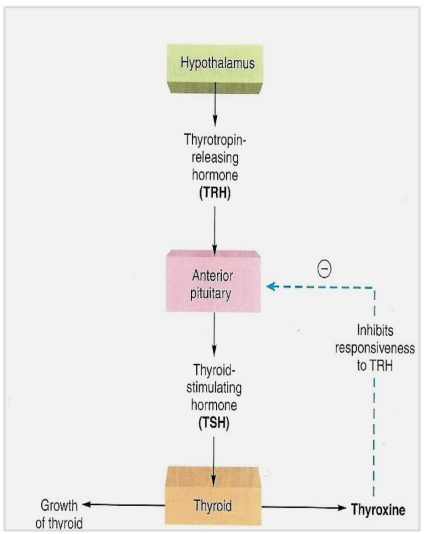
(It is regulated by the hypothalamic-pituitary axis).

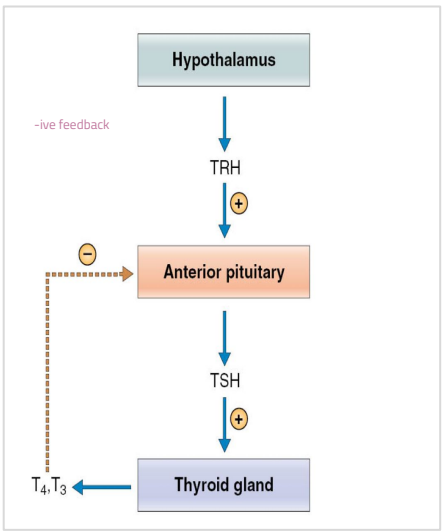
Thyrotropin-Releasing Hormone (TRH):

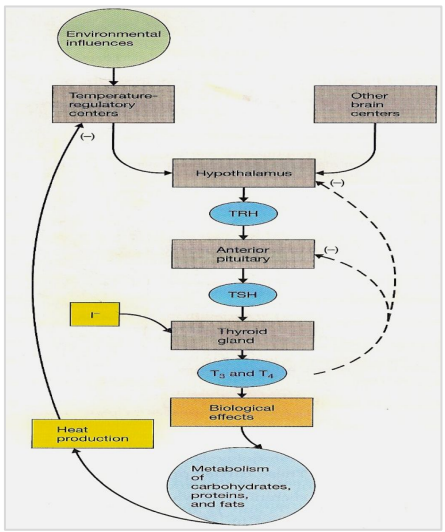
- It's a tripeptide that is released from paraventricular nuclei of the hypothalamus.
- Acts on the thyrotrophs of the anterior pituitary
- Its function is transcription and secretion of TSH.
- Phospholipid second messenger system.*

Thyroid-Stimulating Hormone (TSH):

- It's a **glycoprotein**, released from anterior pituitary.
- It regulates the metabolism, secretion & growth of the thyroid gland **(Trophic effect).**
- Increase the TSH leads to increase release of thyroid hormone and can increase the size of thyroid gland.







- **Hypothalamus releases TRH** which stimulates the anterior pituitary gland to release TSH which stimulates the release of T3 and T4 from the thyroid gland, causing increased metabolism, cardiac output, etc.
- Once there is enough amounts of T3 and T4, they will have a **negative feedback** effect on the anterior pituitary by inhibiting its responsiveness to TRH, thus stopping it from releasing TSH. للمرة المليون نعيدها
- They also have an inhibitory effect on the hypothalamus.
- Some factors like environmental influence (temperature) affect the release of hypothalamic hormone TRH. شلون يالذيب ؟ cold weather stimulate the production thus increase heat....etc
- Iodide has a negative feedback* (remember the Wolff-chaikoff effect?).
- Psychological situation can affect production of thyroid hormones. Depression that why we treat them with thyroxine

* لاحظوا ان الناس اللي يعيشون عند البحر ما عندهم مشاكل بالغدة الدرقية بينما البعيدين عن البحر عندهم تضخم Goiter بسبب زيادة TSH نظرا لقلة اليود. ليش يزيد ال TSH؟ لأن بدون اليود ما نقدر نصنع T4,T3، وبدون T4,T3 ما فيه negative feedback على anterior pituitary فيزيد إفراز ال TSH.

Action of TSH

Important

- TSH secretion starts early at 11-12/13 of the gestational weeks
- TSH increases the synthesis and secretion of thyroid hormones by stimulating almost every step in the biosynthetic pathway:

1- Increase proteolysis of the thyroglobulin.

2-Increase pump activity.

3-Increase iodination of tyrosine.

4-Increase coupling reactions.

5-Trophic effect.
That's why we can see goiter in hypothyroidism

The mechanism of the singling

1. TSH bind to receptor
2. Activation of adenylyl cyclase via Gs protein
3. Increase cAMP (2nd messenger)
4. Increase Activation of protein kinase
5. Multiple phosphorylation reaction
6. Secretion and thyroid growth.

Factors Affecting Thyroid Hormones Secretion

Stimulating factor

- TSH
- Thyroid stimulating immunoglobulins (TSI) → it functions as TSH. found in autoimmune diseases like Graves
- Increased TBG level (e.g. pregnancy)
  (TBG = thyroxine binding globulin)

Inhibiting factor

- Iodide (I-) deficiency.
- Deiodinase deficiency
  (No iodine no thyroid hormone).
- Excessive iodine intake
  (Wolff- Chaikoff effect).
- Perchlorate, thiocyanate
  (inhibits the Na+ , I- Cotransport).
- Propylthiouracil
  (inhibits peroxidase enzyme).
- Decreased TBG levels
  (like liver disease).

Diseases of the thyroid gland (1-Hyperthyroidism)

- Over activity of the thyroid gland.
- Women : Men ratio (8:1).
- **Activity of gland :**
- 5- 10 times increase in secretion Increase in basal metabolic rate because of TSH.
- 2-3 times increase in size (it can be enlarged and smooth or enlarged with lobules)(trophic effect)

Causes:

Important

1- Graves' disease:

- The most common cause.
- An **autoimmune** disorder.
- Increased circulating level of Thyroid-Stimulating Immunoglobulins (**TSI**) (it works same as TSH).
- 95% (Of all causes of hyperthyroidism).
- 4 – 8 times more common in women than men. Almost all autoimmune diseases are more common in females .

2- Thyroid gland tumor:

- The tumor may be in the pituitary or hypothalamus.
- 95% is benign.
- 5% is malignant.
- Definite diagnosis: biopsy
- Predisposing factors:
- History of head and neck irradiation.
- Family history.
- Common in breast cancer patients who had radiation therapy #Med437

3- Exogenous T3 & T4:

- Rare cause.
- Ingestion of excessive amount of thyroid hormone.
- E.g: females used to take thyroxine pills to lose weight

4- Excess TSH secretion:

- Disease of the **Hypothalamus (TRH).**
- Disease of the **pituitary (TSH).**
- They are called **Secondary hyperthyroidism** because they're caused by the pituitary gland or hypothalamus not by thyroid gland.

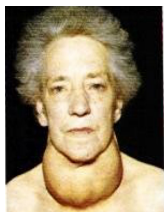
Diagnosis (symptoms) :

How to examine the thyroid gland?
- You can see the enlarged swelling in the thyroid.
- If you ask the patient to drink water you will see the thyroid moving up and down.
- We can differentiate it from thyroglossal cyst that in thyroglossal cyst the thyroid will not move while swallowing but it will move if the patient protrude his tongue.

Case from male dr : A female patient suffering from **sweating** , **weight loss** despite in **increasing of appetite** and increase in the **frequency of going to the bathroom.**

Size:

Goiter (is an abnormal enlargement of thyroid gland) **in 95%.**



- Goiter can be accompanied with :
  1-Normal hormone production 2- Hypo production. 3- Hyper production.

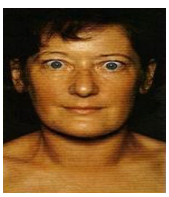
So size has nothing to do with secretion

-Classified according to function (secretion), it can be :
Hyperthyroidism, Hypothyroidism, Euthyroid (Normal thyroid hormone)

Diseases of the thyroid gland (1-Hyperthyroidism)

Diagnosis (symptoms) cont... :

If u understand the Actions u will understand the symptoms

Skin:	- **Smooth, warm and moist** (Moist Because of the increase of metabolism & sweating). - **Night sweating** it's also seen in TB , malaria. - **Heat intolerance** (Because the metabolic rate is high, so the body is burning everything & that produces heat) ايش يعني؟ يعني مايتحمل الحرارة، يكون الشخص في مكان حرارته معتدلة، لكنه حرّان ليش؟ لان الجسم يحرق كل شي يدخله
Musculoskeletal:	- **Muscle atrophy** (caused by ↑ protein catabolic).
Neurological:	- **Tremor.** (First complaint along with palpitations) - **Enhanced reflexes.** - **Irritability** nervous Because of hyper excitability of the whole body.
Cardiovascular:	- **Increase heart rate.** - **Increase stroke volume.** - **Arrhythmias**, **Annoying palpitations** (first complaint) . يحس المريض بدقات قلبه في ظهره و هو ساند ظهره على الكرسي + night palpitations which are extremely specific and differential (all the above are because thyroid hormones potentiate catecholamines). - **Hypertension.**
GI tract:	- Increase in appetite & **Weight loss** caused by ↑BMR "basal metabolic rate". - Malabsorption and increased motility lead to **Diarrhea.**
Renal function:	- **Increased Glomerular filtration rate.** Because it increases CO.
Exophthalmos: جحوظ العين	- Common in Graves disease. - **Anxious staring expression.** - **Protrusion of eyeballs.** - You can see the anxious staring expression, flushed face, goiter Normally the lower eyelid touches the inferior margin of iris and the upper eyelid covers the upper 2 mm of the iris. 
Others:	- **Menstrual cycle disturbance** (In both hypo & hyper).

***Because of tissue deposition behind the eye in the orbit.** Why & How?

- Polysaccharides accumulates behind the eye & it starts to attract water with it, so they push the eye forward.
- TSI will also stimulate the accumulation of these polysaccharides

يعني تتجمع بوليساكرايدز وراء العين وتسحب معاها مويه، تراكمهم راح يدف العين على قدام فيصير جحوظ

Diseases of the thyroid gland (1-Hyperthyroidism)

Investigations:

- **The diagnosis of hyperthyroidism is based on the measurement of T3, T4 and TSH levels.**
- You'll always have high T3 and T4 because its "hyperthyroidism ", the trick is in TSH.

1-primary hyperthyroidism:

In primary hyperthyroidism:

- The disorder is in the thyroid gland.
- There will be high level of T4 and T3, while TSH level will be low by negative feedback of the high level of T3 and T4 on the anterior pituitary. Do u see the trick here??
- High T3, T4 and **Low** TSH → in **primary** hyperthyroidism.
- Why don't we test TRH? Because it's paracrine and won't show up in serum

2-secondary hyperthyroidism:

In secondary hyperthyroidism:

- The disorder is in the hypothalamus or anterior pituitary.
- There will be high level of T4, T3 & TSH.
- increase T3,T4 secretion in response to a high TSH level
- High T3, T4 and **High** TSH → in **secondary** hyperthyroidism.

Treatment:

Medical therapy:	❖ By administration of drugs **e.g. Propylthiouracil,** which inhibit the synthesis of thyroid hormones **(inhibits peroxidase enzymes).** - Usually for 12-18 months course. - **With 3-4 monthly monitoring** (because it we're working according to the feedback mechanism).
Surgery:	❖ **Subtotal thyroidectomy.** In the past it was difficult to treat hyperthyroidism ,they used to remove the parathyroid gland with the thyroid gland , now it is better with the help of the preoperative preparation of the patient also , they leave part of the thyroid gland to protect the parathyroid.
Indication for surgery:	- **Relapse after medical treatment.** No response to the treatment. - **Drug intolerance.** E.g : allergy - **Cosmetic.** شكله قبيح ف في ناس تبي تشيله - **Suspected malignancy.**

❖ Also radioactive iodine is another treatment.
- It destructs the cells which leads to decrease synthesis of the hormones.

Diseases of the thyroid gland (2-Hypothyroidism)

- It is the Under activity of the thyroid gland
- More in **women** (30- 60 years).
- More common than Hyperthyroidism & very common in Saudi Arabia.
- Hypothyroidism diagnosis is frequently confused with depression.
- **Case** from male dr : An **obese** female **always feeling cold** despite the normal temperature and she is suffering from **constipation** as well as **depression.**

Causes:

1- Inherited abnormalities of thyroid hormone synthesis:

- Peroxidase defect.
- Iodide trapping defect.
- Thyroglobulin defect.

يعني محصور في منطقة معينة

2- Endemic Colloid Goiter:

- Is a type of goitre that is associated with dietary iodine deficiency in some isolated communities.
- It used to happen before table salt fortification with Iodine.
- Low Iodine in the blood → Low hormone formation → High TSH → High Thyroglobulin → no Iodide to combine with → Gland thinks there is no Thyroglobulin and increases production further → Increased size (> 10 times)

3- Idiopathic Nontoxic Colloid Goiter:

- Iodine intake is normal.
  E.g: Hashimoto disease
- **Guyton:** Unknown mechanism, but most of the patients show signs of thyroiditis ?
  Proposed Pathogenesis: Inflammation (Thyroiditis) → increased Follicular Cell damage → decreased hormone secretion → increased TSH → increase activity of normal cells → increased Size Due to the trophic effect of TSH. **male dr:** increase in size due to increased demand of the normal cells.
- **Guyton:** This theory could explain why these glands are usually nodular, with some growing portions and some other portions being destroyed.

4- Gland destruction (surgery):

- Although the thyroid have the capacity to grow in response to a stimulus that perturbs the pituitary-thyroid axis, the thyroid gland is considered not a regenerative organ.
- In other word: Surgical removal of the thyroid which will cause hypothyroidism if the patient haven't received the replacement treatment

5- Pituitary diseases or tumor:

No TSH

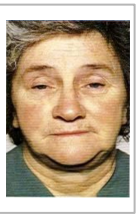
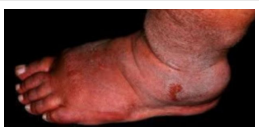
6- Hypothalamus diseases or tumor:

No TRH

Diseases of the thyroid gland (2-Hypothyroidism)

Diagnosis (Symptoms):

- Fine, rough hair, Dull look (sleepy), lack of concentration yellowish skin, Goiter (enlarged thyroid gland).

Skin:	- Dry , rough and thin scaly skin - Cold intolerance. - Pale, tired, dry skin. Sometimes confused with depression, so you must investigate. - Fine and brittle hair, Droopy eyelid , Dull look (sleepy) and Lack of expression, and Yellowish face. 
Musculoskeletal:	- ↑ muscle bulk. - ↓ in skeletal growth. - Muscle sluggishness - Slow relaxation after contraction.
Neurological:	- Slow movement. - Impaired memory. - Decrease mental capacity. } To the degree that it will take you more than one hour just to take the history from the patient.
G.I tract:	- Constipation. - Increase weight. - Decrease appetite
Cardiovascular:	- ↓ Blood volume. - ↓ Heart rate all waves are small in the ECG . - ↓Stroke volume.
Renal Function:	- Decrease glomerular filtration rate. because of the decrease in cardiac output .
Myxoedema:	- An edematous appearance throughout the body. 
Others:	- loss of libido loss of sexual drive. - Menstrual cycle disturbance or infertility. - Frog-like, husky sound.

How does she look?

تعبانة، نعسانة، خاملة أغلب الوقت، مكتئبة ومالها خلق شيء

- So hypothyroidism & depression have similar signs that's why we **must do thyroid function tests (TFT) to differentiate between them.**
- A differential diagnosis of hypothyroidism is depression.

Diseases of the thyroid gland (2-Hypothyroidism)

Investigations:

- The diagnosis of hypothyroidism is based on the measurement of T3, T4 and TSH levels.
- You'll always have low T3 and T4 because its "hypothyroidism ", the trick is in TSH.

1

I- Serum T3,T4:
- Low

2

2- Serum TSH:
- Elevated in primary hypothyroidism (There is low amount of T3 and T4 secreted, so the pituitary thinks that it's not secreting enough TSH, so it will increase the secretion of TSH). the opposite of hyper
- Low in secondary hypothyroidism because here, what caused hypothyroidism is low TSH or TRH level.

Treatment:

L-Thyroxine

- It is a Hormone replacement therapy, MUST monitor & adjust dose.
- Starting dose is 25-50 µg. We increase the dose 25-50 µg per month
- Increase to 200 µ.. in most patients the appropriate dose ranges between (100,125,150) it depends on patients lifestyle, for example, In young active female:150-200 and in old age female:100
- At 2-4 weeks period.

(The first response seen is the weight loss).

Cretinism (التقزم)

- It is the Extreme hypothyroidism during infancy and childhood (failure of growth).
(Inability to secrete the thyroid hormone. Thyroid hormone isn't there → An important stimuli of the GH).

Causes:

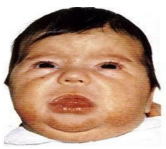
1. Congenital lake of thyroid gland (congenital cretinism). This is why postnatal screening for thyroid hormone is very important
2. Genetic deficiency leading to failure to produce hormone.
Such peroxidase, thyroglobuline defect
3. Iodine lake in the diet (Endemic cretinism).

Cretinism (التقزم)

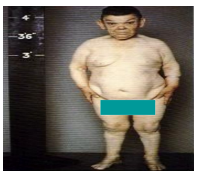
Symptoms:

Infant is normal at birth but abnormality appears within weeks.

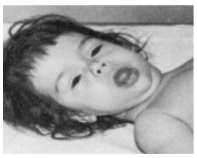
Protruding tongue, microcephaly.



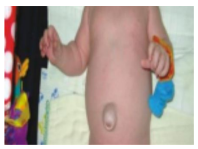
Dwarf with short limbs.



Mental retardation.



Often umbilical hernia.*



Teeth changes*

Dwarf + Mental retardation= Cretinism*
Note: GH deficiency result in short stature (dwarfism), but CNS maturation is normal

Treatment:

- Changes are **irreversible** unless treatment is given early. So early treatment is so important

Female slides

For your knowledge

Calculate your BMR:

Men: BMR = 66 + (13.7 X wt in kg) + (5 X ht in cm) - (6.8 X age in years)

Women: BMR = 655 + (9.6 X wt in kg) + (1.8 X ht in cm) - (4.7 X age in years)

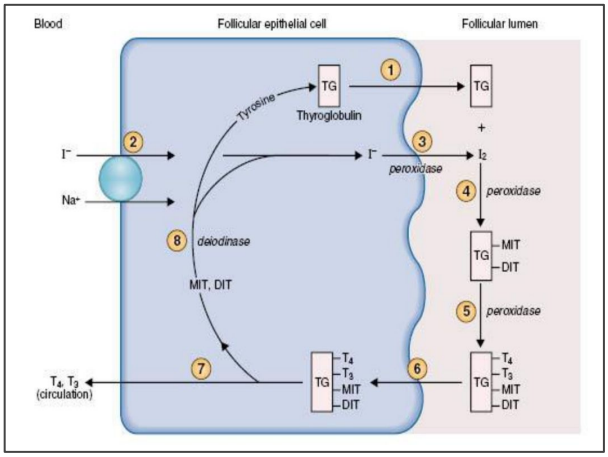
Example:
You are female
You are 30 years old
You are 5' 6 " tall (167.6 cm)
You weigh 120 lbs. (54.5 kilos)

Your BMR = 655 + 523 + 302 - 141 = **1339 calories/day**

All found in Slides

Summary of Biosynthesis of Thyroid Hormones

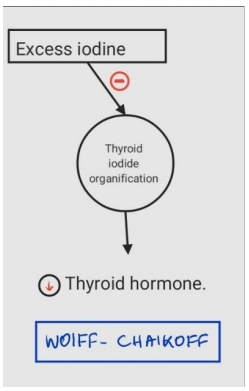
هذا اللي اقصده لل Steps بعد ما تقرأ الخطوات شوفها هنا



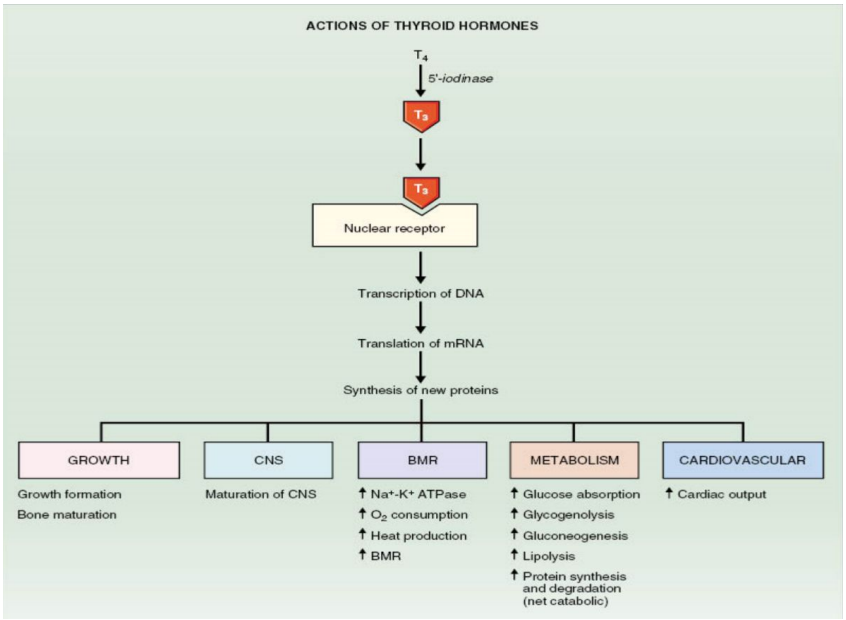
Event	Site	Enzyme	Inhibitor
1 Synthesis of TG; extrusion into follicular lumen	Rough ER, Golgi apparatus		
2 Na^+ - I^- cotransport	Basal membrane		Perchlorate, thiocyanate
3 Oxidation of $I^- \rightarrow I_2$	Apical (luminal) membrane	Peroxidase	PTU
4 Organification of I_2 into MIT and DIT	Apical membrane	Peroxidase	PTU
5 Coupling reaction of MIT and DIT into T_3 and T_4	Apical membrane	Peroxidase	PTU
6 Endocytosis of TG	Apical membrane		
7 Hydrolysis of T_4 and T_3; T_4 and T_3 enter circulation	Lysosomes	Proteases	
8 Deiodination of residual MIT and DIT Recycling of I^- and tyrosine	Intracellular	Deiodinase	

Propylthiouracil

Wolff-chaikoff effect

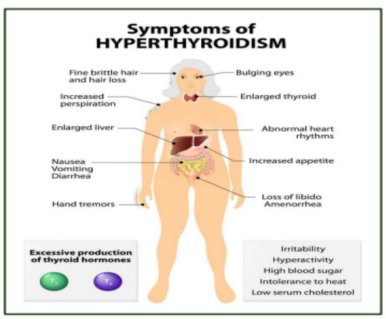


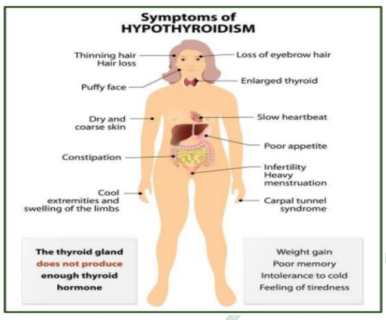
Summary of Action of Thyroid Hormones



Summary of Action of Thyroid Hormones

	Hyperthyroidism	Hypothyroidism
Symptoms	Increased basal metabolic rate Weight loss Negative nitrogen balance Increased heat production Sweating Increased cardiac output Dyspnea (shortness of breath) Tremor, muscle weakness Exophthalmos Goiter	Decreased basal metabolic rate Weight gain Positive nitrogen balance Decreased heat production Cold sensitivity Decreased cardiac output Hypoventilation Lethargy, mental slowness Drooping eyelids Myxedema Growth retardation Mental retardation (perinatal) Goiter
Causes	Graves' disease (increased thyroid-stimulating immunoglobulins) Thyroid neoplasm Excess TSH secretion Exogenous T_3 or T_4 (factitious)	Thyroiditis (autoimmune or Hashimoto's thyroiditis) Surgery for hyperthyroidism I^- deficiency Congenital (cretinism) Decreased TRH or TSH
TSH Levels	Decreased (feedback inhibition of T_3 on the anterior lobe) Increased (if defect is in anterior pituitary)	Increased (by negative feedback if primary defect is in thyroid gland) Decreased (if defect is in hypothalamus or anterior pituitary)
Treatment	Propylthiouracil (inhibits peroxidase enzyme and thyroid hormone synthesis) Thyroidectomy $^{131}I^-$ (destroys thyroid) β-Adrenergic blocking agents (adjunct therapy)	Thyroid hormone replacement therapy





Answers :1 -D/ 2-D/ 3-D/4-B/ 5-A/ 6-C/ 7-C/ 8-D/9- A

MCQs:

QI: I:which one of the following is not unique features of thyroid gland?

A- Contains a large amount of iodine supplied in diet | B- Synthesis is partially intracellular and partially extracellular | C- T4 is the major product | D- T3 is the major product

Q2: where does the Thyroglobulin formation take place?

A- rough endoplasmic reticulum | B- Golgi apparatus | C-nucleus | D- A&B

Q3: :which of the following is the effect of thyroid hormone in carbohydrates metabolism ?

A- decrease glucose uptake by cells | B- decrease glycogenolysis | C- decrease absorption of the GI tract | D- increase glycogenolysis

Q4: A 34 year-old women complains of a bulge on her neck that has developed over the past few months. The patient also complains of heat-intolerance and weight loss. Physical examination reveals exophthalmos.Her TSH level is 0.I µU/mL What is the diagnosis?

A- Hypothyroidism. | B- Hyperthyroidism. | C- Pituitary adenoma | D-Hypothalamus disorder.

Q5: Case A female patient suffering from sweating , weight loss despite in increasing of appetite and increase in the frequency of going to the bathroom what is the diagnosis?

A- Hyperthyroidism. | B- Hypothyroidism. | C- Cushing's syndrome | D- Addison's disease

Q6: which one of the following stimulate thyroxine?

A- high temperature | B- radiation therapy | C- Pregnancy | D- partial thyroidectomy

Q7:Case An obese female always feeling cold despite the normal temperature and she is suffering from constipation as well as depression what is the diagnosis?

A- Hyperthyroidism. | B- Cushing's syndrome | C- Hypothyroidism. | D- Addison's disease

Q8: which one of the following is a sign of a primary hyperthyroidism?

A- hypertension | B- decreased cardiac output | C- decreased metabolic rate | D- weight loss

Q9: which one of the following is a feature of cretinism?

A- Mental retardation | B-hypocholesterolemia | C- increase basal Metabolic rate | D- small tongue

SAQ:

QI. List the steps of thyroid hormones biosynthesis?

Q2. Explain Wolff-chaikoff effect?

Q3. List 4 causes of hyperthyroidism?

AI. I- iodide pump. 2- Thyroglobulin synthesis. 3-Oxidation of iodide to iodine. 4- Iodination. 5- coupling. 6-Endocytosis . 7-Fusion of lysosomes with vesicles. 8- hydrolysis of the peptide bond in thyroglobulin. 9- Release of T3/T4

A2. A reduction in thyroid hormone levels caused by administration of a large amount of iodine.

A3. -Graves' disease. -Thyroid neoplasm -Exogenous T3/T4. -Excess TSH secretion.

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Special thanks to notes taker Lama Al Mutairi and Yazeed Al Sulaim and Fahad Al Mughaiseeb