

# Endocrine Block

"إن الله لا يُعطي  
أصعب المعارك، إلا  
لأقوى جنوده"

- Text
- Only in Females' slide
- Only in Males' slides
- Important
- Numbers
- Doctor notes
- Extra Notes



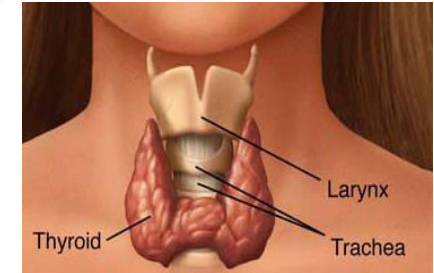
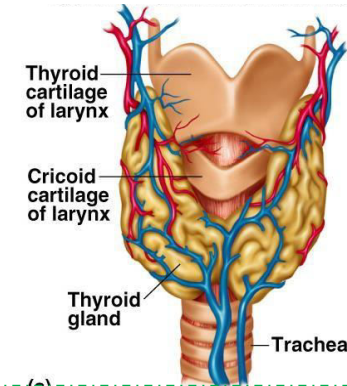
# Physiology & Diseases of the thyroid gland

By the end of this lecture, students should be able to describe:

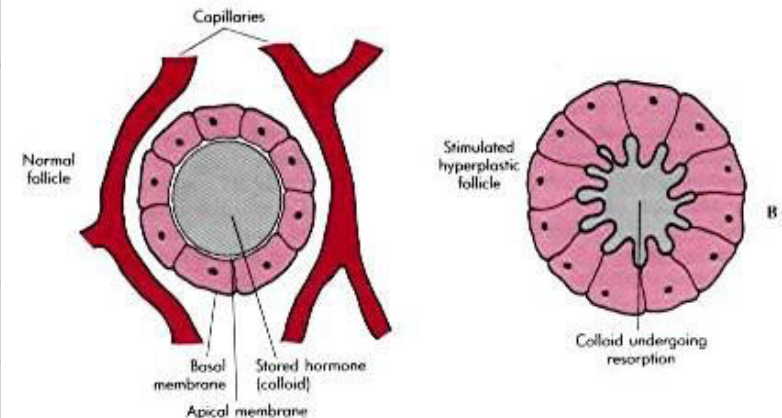
1. List thyroid gland hormones.
2. Describe the synthesis of the thyroid hormones.
3. Describe the release and actions of thyroid hormones.
4. Describe the negative feedback mechanism (control).
5. Describe pathophysiology behind the causes of hyper-hypothyroidism.
6. Describe pathophysiology behind the signs and symptoms of hyper-hypothyroidism.
7. List the treatment.

# Thyroid Gland

- ▶ It is located below the larynx on either sides & anterior to the trachea (It is not attached to larynx, its only lies above it)
- ▶ The first recognized endocrine gland, but the master one is pituitary gland.
- ▶ 20g in adult.



Highly vascularized



- ✓ Thyroid gland is made of follicles.
- ✓ Follicles are lined by follicular cells.
- ✓ The surrounded pinkish material is colloid

Thyroid gland hormones				
الكمية عكس الactivity، يعني كلما زادت الكمية قل نشاط الهرمون (أقلهم كمية أكثرهم نشاطا)				
Hormones	<b>T3</b> (Triiodothyronine)	<b>T4</b> Thyroxine (Tetraiodothyronine)	<b>Calcitonin</b> Hormone important in Ca metabolism.	<b>Reverse T3</b> (not important) Biologically inactive, but it appears in chemical reactions
Amount	10%	90%	-	-
Site of synthesis	Apical and basal membrane in follicular cells		Parafollicular cells C-cell	-
Site of stores	In colloid			-

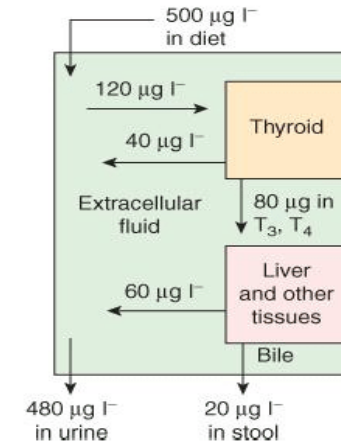
# Unique features of thyroid gland

## 1. Contains a large amount of iodine:

- supplied in diet موجود في ملح الطعام
- 1 mg/week.

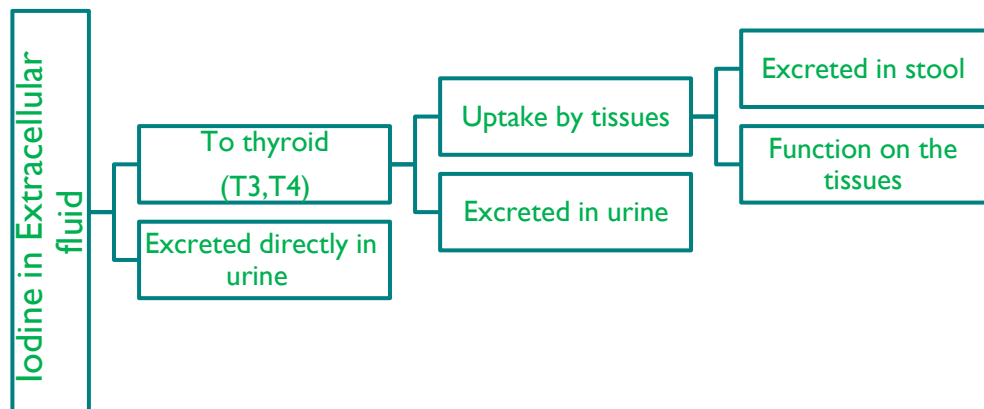
## 2. Synthesis is partially intracellular & partially extracellular (One special thing in thyroid hormones is that part is synthesized inside the cells and some outside the cells).

## 3. T4 is the major product (But less active).



Pic is Only in Females' Slides

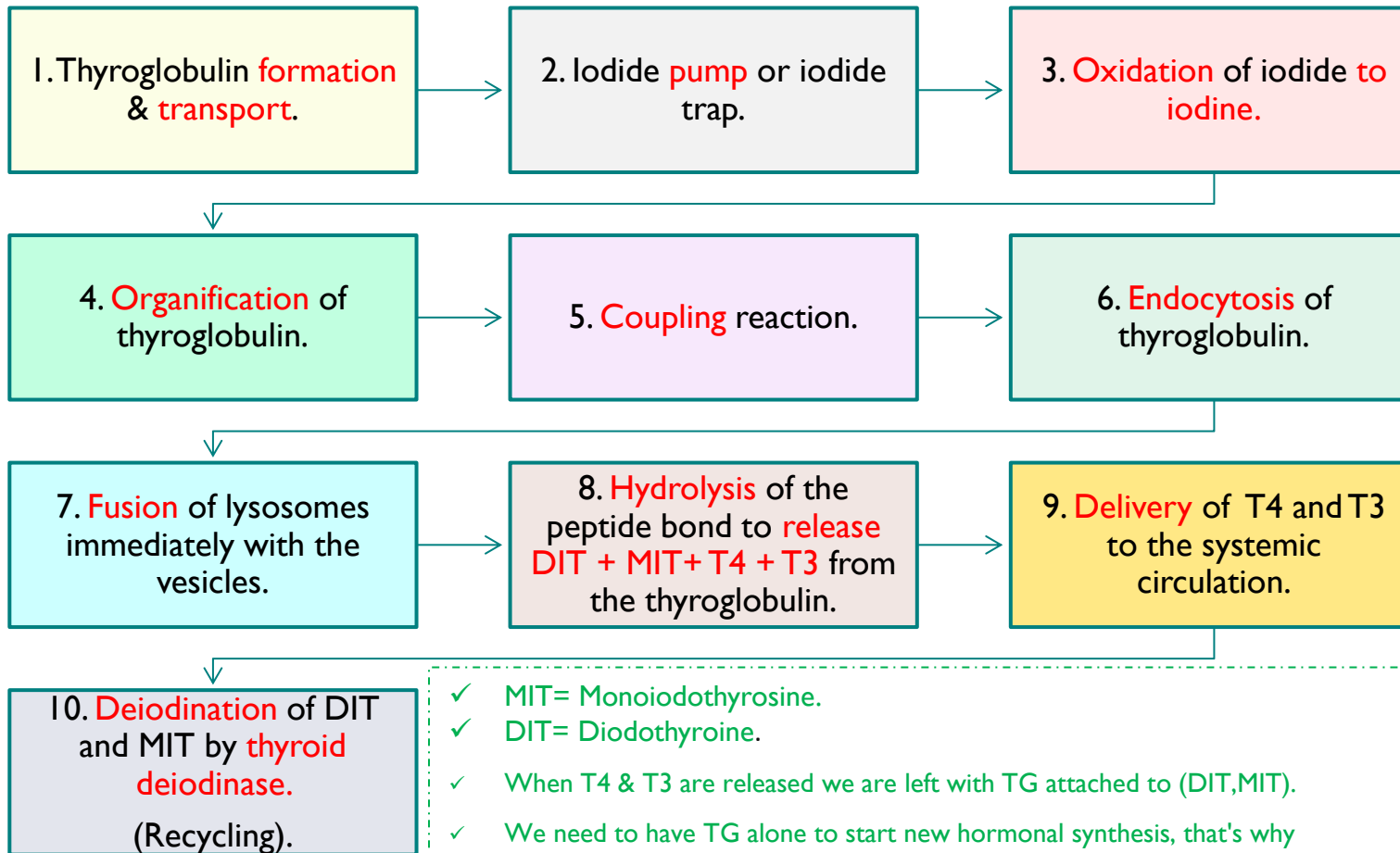
**FIGURE 19-5 Iodine metabolism.** The figure shows the movement of iodide amongst various body compartments on a daily basis.



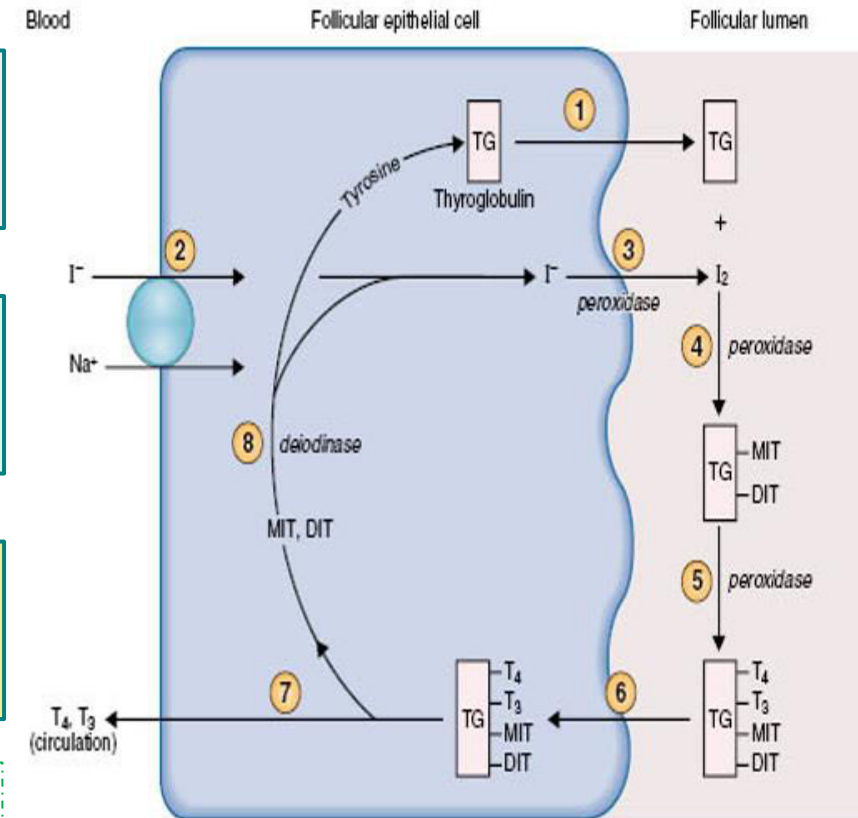
- ✓ 500Mg iodine is uptake by diet enters the circulation.
- ✓ 120Mg (large amount) is taken up by thyroid gland for thyroid hormones synthesis (T3 ,T4).
- ✓ Some is taken by liver and other tissues:
  - 20% of the Iodide is taken by the thyroid gland.
  - while remaining 80% will be excreted in urine.

# Steps in Biosynthesis of Thyroid Hormones

There are 10 steps in biosynthesis of thyroid hormones done by the follicular cells:



- ✓ MIT= Monoiodothyrosine.
- ✓ DIT= Diodothyrosine.
- ✓ When T4 & T3 are released we are left with TG attached to (DIT,MIT).
- ✓ We need to have TG alone to start new hormonal synthesis, that's why (DIT,MIT) will be removed by the action of deiodinase to have TG to start synthesizing new thyroid hormones.



Other picture

Another Picture

# Cont.

## 1. Thyroglobulin Formation & Transport:

- ✓ Thyroglobulin is formed of **140** tyrosine (main amino acid) + **glycoprotein**. (glycoprotien = protien + caebohydrate)
- ✓ It is formed in Rough endoplasmic reticulum & Golgi apparatus.

## 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.

## 2. Iodide Pump Or Iodide Trap:

- ✓ Iodide is very essential component for thyroid hormones, T4 contains 4 iodine & T3 contains 3.
- ✓ Active transport (Which is sodium iodide co-transporter).
- ✓ Wolff-chaikoff effect\*.

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

تطبيق لنظرية العرض والطلب: الحين لما الناس تسمع عن سلعة بتخلص لأنهم يراكون عشان يشترونها، نفس الشي لما يوصل اليود للدم يكون قليل، هذا بيأثر على نشاط ال Pump يزيد ويأخذ كل اليود الموجود والعكس صحيح.

في السابق كانوا يستخدمون هذه الطريقة للعلاج (Negative feedback) (وداوها بالتي كانت هي الداء)

- ✓ Ratio of concentration from **30-250** times (in the gland compared to the blood).
- ✓ It is stimulated by TSH (The pump number & activity will be increased in response to TSH).

Wolff-chaikoff effect: **Read it**

- ✓ when Iodide in blood is increased, the number & activity of Iodide pump will be decreased because there is abundant Iodide in blood.
- ✓ While when Iodide in blood is decreased, the number & the activity of this pump will be increased to uptake this small quantity of Iodide in blood.

# Cont.

## 4. Organification Of Thyroglobulin:

- ✓ Binding of iodine with Thyroglobulin.
- ✓ Catalyzed by **thyroid peroxidase** to formation of MIT & DIT.
- ✓ Remain attached to thyroglobulin until the gland stimulated to secret.
- ✓ MIT= Monoiodothyrosine & DIT= Diodothyroine.
- ✓ 1 Tyrosine of Thyroglobulin + 1 Iodine = MIT.
- ✓ 1 Tyrosine of Thyroglobulin + 2 Iodine = DIT.
- ✓ Thyroglobulin is formed from tyrosine, this tyrosin can attach to one iodine (MIT) or 2 iodine (DIT).

## 5. Coupling Reaction:

- ✓  $DIT + DIT = T4$  (faster), while  $DIT + MIT = T3$
- ✓ Catalyzed by **thyroid peroxidase**.
- ✓ It is stored as colloid.  
 عندنا follicular cell وفي النص الهرمون as a colloid واذا احتجته اسوي endocytosis، هل ينفع يطلع للدم؟ لا، اكسره واطلع t3 و t4.
- ✓ Is sufficient for **2-3 months** (That's why hypo/ hyper thyroidism symptoms will appear late)

## 6. Endocytosis of Thyroglobulin.

After formation & entering the colloid endocytosis of thyroglobulin starts.

## 7. Fusion Of Lysosomes Immediately With The Vesicles.

If it enters follicular cells the lysosomes bind with vesicles and hydrolysis occurs.

## 8. Hydrolysis (proteolysis) Of The Peptide Bond To Release DIT + MIT+ T4 + T3 From The Thyroglobulin.

- ✓ MIT= Monoiodothyrosine.
- ✓ DIT= Diodothyroine.

## 9. Delivery Of T4 and T3 to The Systemic Circulation.

By concentration gradient → target cells → action.

## 10. Deiodination of DIT And MIT By **Thyroid Deiodinase** (recycling).

(Deiodination is a process of separating the Iodine and Tyrosine in DIT & MIT to use Tyrosine again in synthesis of Thyroglobulin & also to reuse the Iodine).

# Thyroid Hormones in The Circulation

1. Unbound (**free**): Found in small amounts.

▶ 0.03% of T4.

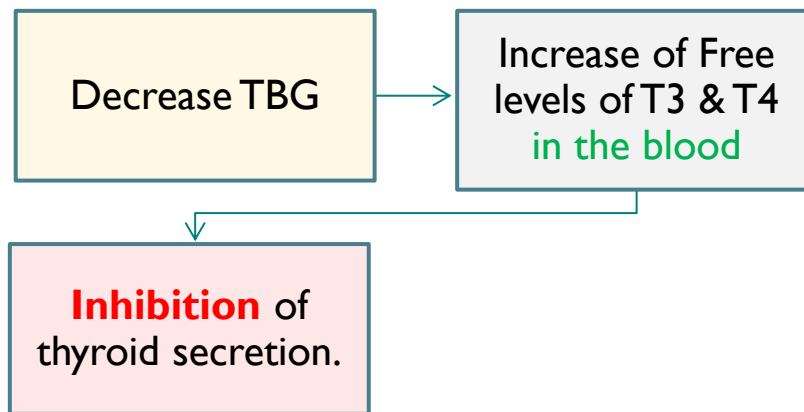
▶ 0.3% of T3 (more, because it's the needed form, Free hormone it's the only type that triggers negative Feedback and it is the active form).

✓ Bound hormones inactive → type of storage.

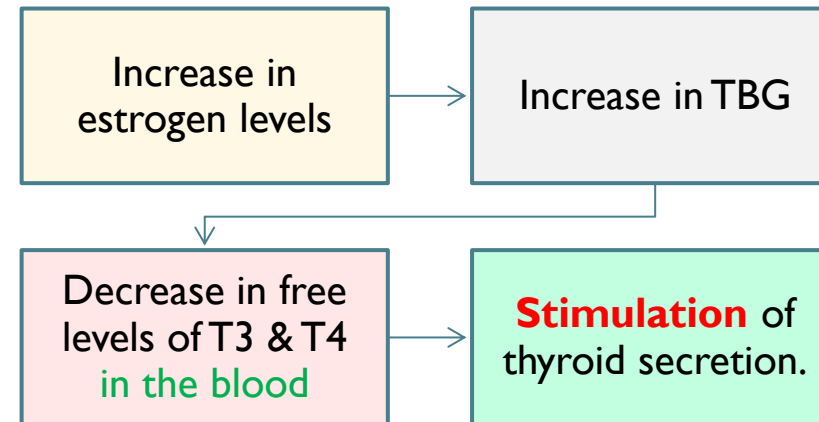
✓ Unbound hormones active → less amount.

2. Bound: 70-80% is bound to thyroxine-binding globulin (TBG) which is **synthesized in the liver**, the reminder is bound to albumin.

▶ Effect of Liver diseases (Hepatic failure) on thyroid hormones:



▶ Effect of pregnancy on thyroid hormones:



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.

pregnant women feels hot due to increase T3 & T4.



# Release of T4 & T3 Into The Tissues

1. The release is **slow** because of the high affinity of the plasma binding proteins.

▶  $\frac{1}{2}$  of T4 in the blood is released every **6** days &  $\frac{1}{2}$  of T3 in the blood is released every **one** day.

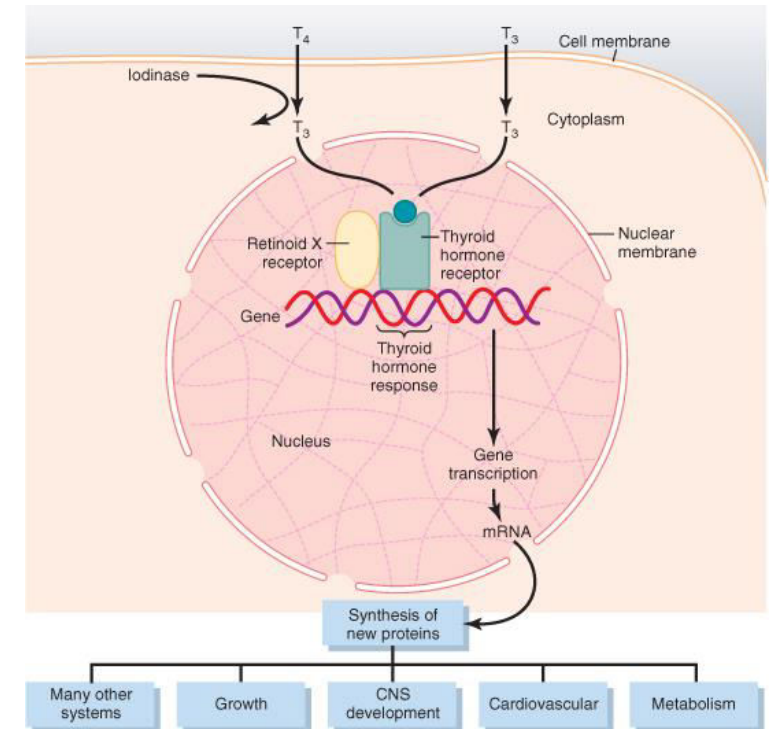
2. T4 & T3 readily diffuse through the cell membrane.

3. It is stored in the targeted tissues (days to weeks).

4. Most of T4 is deionized to T3 by **5-iodinase enzyme** (Before binding to the nuclear receptors  
90% of T4 is converted to T3)

5. In the nucleus, T3 mainly binds to “thyroid hormone receptor” & influence transcription of genes.

T3, T4 can easily enter cell membrane → to cytoplasm → iodinase converts T3 to T4 → T3 enters the nuclear membrane → nucleus → bound to thyroid hormone receptor → manipulated DNA synthesis and mRNA → gives protein that has affect on target cells. it enters the Cell membrane, Nuclear membrane & stimulates the synthesis of certain proteins.



T3 binds to the nuclear receptor forming a T3-receptor complex

Activation of thyroid regulating element on the DNA

DNA transcription → formation of mRNA

Translation of mRNA → specific **protein synthesis** (target tissue specific).

# Action of thyroid hormones

Thyroid hormones affect many systems because they affect the metabolism and all cells have metabolism

## Action of thyroid hormones

Effect on Autonomic nervous system	Effect on CNS These effects are age dependent:		Effect on Respiration
<ul style="list-style-type: none"> <li>✓ Thyroid hormone interact with the sympathetic nervous system.</li> <li>✓ Produced the same action as catecholamine's via <math>\beta</math> adrenergic receptors including increase:</li> <li>A. BMR.</li> <li>B. Heat production.</li> <li>C. Heart rate.</li> <li>D. Stroke volume.</li> </ul> <p>.i.e. <math>\beta</math>-blocker (propranolol) is used in treatment of hyperthyroidism.</p>	fetal and postnatal life	<ul style="list-style-type: none"> <li>✓ Thyroid hormones are essential for maturation of the CNS.</li> <li>✓ perinatal decrease of hormones secretion (hypothyroidism) causes irreversible mental retardation. For this reason, screening is necessary to introduce hormone replacement.</li> <li>✓ If it is detected in the new born, hormone replacement can reverse the CNS effect.</li> <li>✓ If the baby isn't responsive, inactive, sleeps a lot = thyroid hormone deficiency.</li> </ul>	<ol style="list-style-type: none"> <li>1. Increase ventilation rate.</li> <li>2. Increase dissociation of oxygen from Hb by increasing red cells 2,3-DPG (2,3diphosphoglycerate).</li> </ol> <p>2,3-DPG will decrease the affinity of the RBC, &amp; increase the loading to the tissues.</p>
In adult	<p><b>Increase in thyroid hormone secretion:</b> (Hyperthyroidism = tremor)</p> <ol style="list-style-type: none"> <li>1. Hyperexcitability.</li> <li>2. Irritability.</li> </ol> <p><b>Decrease in thyroid hormones secretion:</b> عكس الهايبر</p> <ol style="list-style-type: none"> <li>1. Slow movement.</li> <li>2. Impaired memory.</li> <li>3. Decrease Mental capacity.</li> </ol>		

# Cont.

## Action of thyroid hormones

Basal metabolic rate (BMR) = The amount of energy the body needs to maintain basal functions. بعدها الجسم خلاص هضم وتخلص من الجلوكوز BMR هو كمية الطاقة الاساسية الموجودة.	Effect on Metabolism		
	Affect on carbohydrate metabolism	Effects on fat metabolism	Effect on protein metabolism
<ul style="list-style-type: none"> <li>✓ It is the energy requirement under basal or resting condition (state of mental &amp; physical rest 12-18 hours after a meal).</li> <li>✓ Complete lack of the thyroid hormones → decreases BMR 40% - 50%. (If there is no thyroid hormones energy amount decrease to half)</li> <li>✓ Extreme increase of the thyroid hormones → increases BMR 60-100% (If there is thyroid hormone excess the amount of energy is doubled, Because it affects O<sub>2</sub> consumption in cells).</li> </ul> <p>الخلايا لها سرعة حركة معينة ممكن تزيد وممكن تقل، عشان تستمر الحركة نحتاج طاقة، لما تقعد مريح ١٣-١٦ ساعة بعد الوجبة الجسم بيحتاج هالمصدر من الطاقة.</p>	<p>Increase:</p> <ol style="list-style-type: none"> <li>1. Glucose uptake by the cells.</li> <li>2. <b>Glycogenolysis.</b></li> <li>3. <b>Gluconeogenesis.</b></li> <li>4. Absorption from the GIT.</li> </ol>	<ol style="list-style-type: none"> <li>1. Increase lipolysis.</li> <li>2. Decrease plasma cholesterol by increase loss in feces.</li> <li>3. Increase oxidation of free fatty acids. التايرود يحرق الدهون، عشان كذا بعض السنتات ياخذون التايركسون عشان يخسوا (ينحفوا) بس أو عكم تعملوها لأن اللعب بالهرمونات زي اللعب بالنار، هتنبسطوا أول يومين وبعدها تعيطوا.</li> </ol>	<p>Overall effect is catabolic leading to decrease in muscle mass.</p> <p>هذي المرحلة يكون الجسم اكل الجلوكوز و اكل الدهون بقى العضلات.</p>
<p>The metabolic effects are due to the induction of metabolic enzymes:</p> <ol style="list-style-type: none"> <li>1. Cytochrome oxidase.</li> <li>2. NADPH cytochromeC reductase.</li> <li>3. Alpha-glycerophosphate dehydrogenase.</li> <li>4. Malic enzymes.</li> <li>5. Several proteolytic enzymes.</li> </ol> <p style="border: 1px dashed red; padding: 5px; display: inline-block;">الدكتورة قالت مو مهم، والدكتور ما شرحها</p>			

# Cont.

## Action of thyroid hormones

Effects on the cardiovascular system	Effect on GIT	Bone (growth hormone)
<p>✓ Increase heart rate &amp; stroke volume (increased contractility) Which lead to raises the <b>Cardiac out put up to 60%</b> → increase delivery of <b>oxygenated</b> blood to the tissues.</p> <p>✓ Decrease peripheral resistance → increase delivery of <b>oxygenated</b> blood to the tissues. Why there is peripheral resistance? Increased metabolism in the tissues causes more rapid decrease utilization of oxygen than normal &amp; release of greater than normal quantities of metabolic end products from the tissues. These effects cause vasodilation in most body tissues, thus increasing blood flow.</p> <p><b>How do the thyroid hormones perform their effects on CVS?</b> The increased contractility is partly direct and partly indirect:</p> <p>1. <b>Indirect:</b> Thyroid hormones potentiate the effect of catecholamine in the circulation → activation of <math>\beta</math>-adrenergic receptors.</p> <p>2. <b>Direct induction of:</b></p> <ol style="list-style-type: none"> <li>1. <b>Myocardial <math>\beta</math>-adrenergic receptors.</b></li> <li>2. <b>Sarcoplasmic reticulum.</b></li> <li>3. <b>Ca<sup>2+</sup> ATPase.</b></li> <li>4. <b>Myosine.</b></li> </ol>	<p><b>Increase:</b></p> <ol style="list-style-type: none"> <li>1. Appetite and food intake.</li> <li>2. Digestive juices secretion.</li> <li>3. G.I tract motility:           <ul style="list-style-type: none"> <li>✓ <b>excess secretion causes <u>diarrhea</u></b> → hyperthyroidism.</li> <li>✓ <b>lack of secretion causes <u>constipation</u></b> → hypothyroidism.</li> </ul> </li> </ol> <p>Hyperthyroidism = <b>increase</b> appetite and <b>loss</b> of weight. Hypothyroidism = <b>decrease</b> appetite and <b>gain</b> weight.</p>	<p><b>Promote:</b></p> <ol style="list-style-type: none"> <li>1. Bone formation &amp; maturation.</li> <li>2. Ossification.</li> <li>3. Fusion of bone plate.</li> </ol> <p>We said promote because the action is done by growth hormone.</p>

# Regulation of Hormones secretion

Regulation of Hormones secretion:

It is regulated by the hypothalamic-pituitary axis.

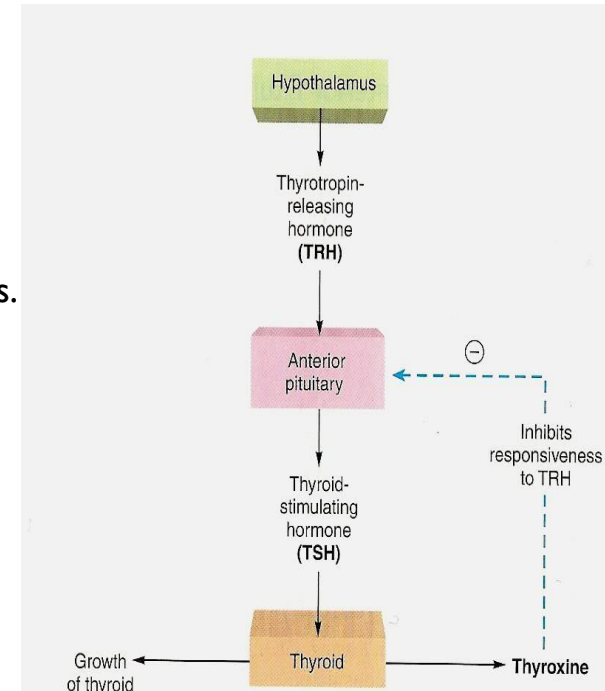
## 1. Thyrotropin-releasing hormone (TRH):

- ▶ It's a tripeptide, released from the paraventricular nuclei of the hypothalamus.
- ▶ It acts on the thyrotrophs of the anterior pituitary.
- ▶ Its function is transcription & secretion of TSH.
- ▶ Phospholipid second messenger system.

## 2. Thyroid-stimulating hormone (TSH):

- ▶ It's a glycoprotein, released from the anterior pituitary.
- ▶ It regulates the metabolism, secretion & growth of the thyroid gland (Trophic effect).

- ✓ The hypothalamus secretes TRH to the Anterior pituitary glands which stimulates it into secreting TSH into the thyroid gland which leads to release of T3 & T4.
- ✓ Once there is enough amounts of T3 and T4 it will inhibit the responsiveness of the anterior pituitary to TRH, thus stopping it from releasing TSH.



- ✓ Hypothalamus releases TRH which stimulates the anterior pituitary gland to release TSH which stimulates the release of T3 and T4 from the thyroid gland.
- ✓ T3 and T4 have a negative feedback effect on the anterior pituitary.
- ✓ Some factors like environmental influence (temperature) affect the release of hypothalamic hormone TRH.

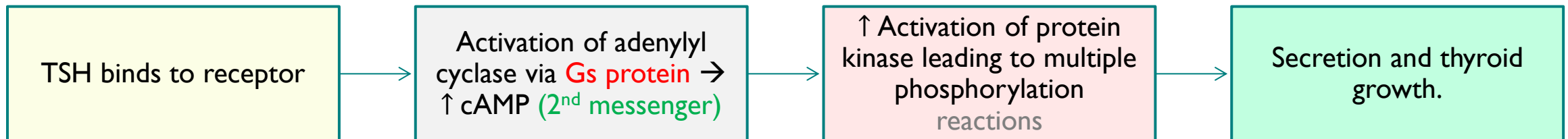
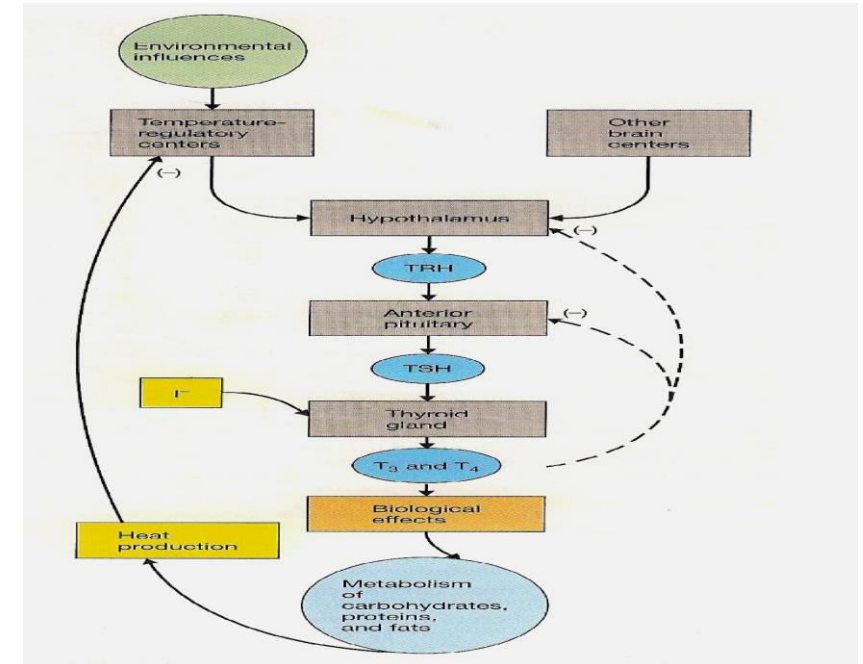
# Action of TSH

TSH secretion started at 11-13 of gestational weeks.

## ▶ Action of TSH

1. It increases proteolysis of thyroglobulin.
2. Increases pump activity to increase iodide entering the cell.
3. Increases iodination of tyrosine.
4. Increases coupling reaction.
5. Trophic effect.

لاحظوا ان الناس اللي يعيشون عند البحر ما عندهم مشاكل بالغدة الدرقية بينما البعيدين عن البحر عندهم تضخم  
Goiter بسبب زيادة TSH.



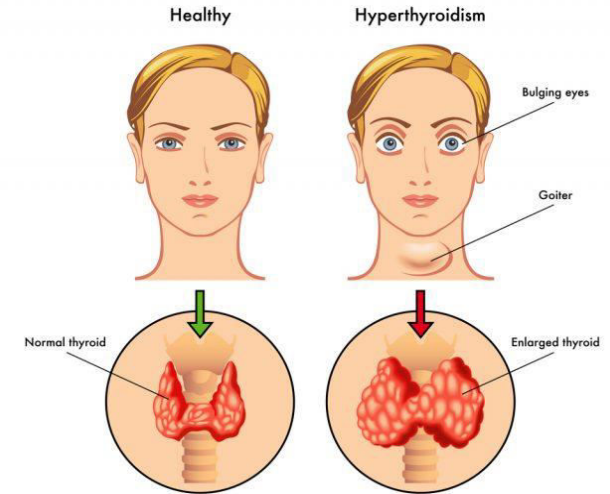
# Factors affecting thyroid hormones secretion

Factors affecting thyroid hormone secretion	
Stimulating factors	Inhibiting factors
<ol style="list-style-type: none"><li>1. TSH.</li><li>2. Thyroid stimulating immunoglobulin (TSI) → it functions as TSH.</li><li>3. Increase TBG levels (like pregnancy).</li></ol>	<ol style="list-style-type: none"><li>1. Iodide (I<sup>-</sup>) deficiency.</li><li>2. Deiodinase deficiency (No iodine no thyroid hormone).</li><li>3. Excessive iodide intake (wolff-chaikoff effect).</li><li>4. Perchlorate, thiocyanate (inhibits the Na<sup>+</sup>, I<sup>-</sup> Cotransport).</li><li>5. Propylthiouracil (inhibits peroxidase enzyme).</li><li>6. Decreased TBG levels (like liver disease).</li></ol>

Hyperthyroidism = excessive secretion of hormones stimulated by immunoglobulin instead of hormones (Autoimmune disease) Ig mimics TSH.

# Hyperthyroidism

- ▶ **Definition:** Over activity of the thyroid gland.
- ▶ More common in **Women**, Women:men ratio (**8:1**).
- ▶ Increase activity of the gland, what does it mean?
  - A. **5- 10** times increase in secretion **because of TSH**.
  - B. **2-3** times increase in size **because of trophic effect**.



## Causes

### 1. Graves' disease

- ✓ The most common cause.
- ✓ An autoimmune disorder.
- ✓ Increased circulating level of thyroid stimulating immunoglobulins (TSI).
- ✓ **95%** (Of all causes of hyperthyroidism).
- ✓ **4 – 8 times more common in women than men.**



### 2. Thyroid gland tumor

- ✓ The tumor may be in the pituitary or hypothalamus.
- ✓ **95%** is benign & **5%** is malignant.
- ✓ History of head & neck irradiation & family history.

### 3. Exogenous T3 and T4

- ✓ rarely cause.
- ✓ eg. in case of hypothyroidism treatment.


بعض الناس يأخذونهم كحبوب  
لنقص الوزن.

### 4. Excess TSH secretion


- ✓ Diseases of the hypothalamus (TRH).
- ✓ Diseases of the pituitary (TSH).



# Diagnosis (Signs and symptoms) تجيك وحده، خففت ملابسها، رايحه جايه على دورة المياه و نحيفه.

<p>Size</p>	<ul style="list-style-type: none"> <li>✓ Goiter (is an abnormal enlargement of thyroid gland) in 95%.</li> </ul> 	<p>Cardiovascular</p>	<ul style="list-style-type: none"> <li>✓ Increase heart rate &amp; stroke volume.</li> <li>✓ Arrhythmias</li> </ul> <p>(all the above are Because thyroid hormone potentiate catecholamines).</p> <ul style="list-style-type: none"> <li>✓ Hypertension.</li> </ul>
<p>skin</p>	<ul style="list-style-type: none"> <li>✓ Smooth, warm &amp; <u>moist</u> رطب (Moist Because of the increase of metabolism &amp; sweating).</li> <li>✓ Heat intolerance &amp; night sweating. (Because the metabolic rate is high, so the body is burning everything &amp; that produces heat).</li> </ul> <p>ايش يعني؟ يعني مايتحمل الحرارة. يكون الشخص في مكان حرارته معتدله، لكنه حرّان ليش؟ لأن الجسم يحرق كل شيء يدخله.</p>	<p>G.I tract</p>	<ul style="list-style-type: none"> <li>✓ Increase in appetite &amp; weight loss caused by ↑ BMR “basal metabolic rate”.</li> <li>✓ Malabsorption lead to Diarrhea.</li> </ul>
		<p>Renal function</p>	<ul style="list-style-type: none"> <li>✓ Increase glomerular filtration rate.</li> </ul>

# Cont.

<p>Musculoskeletal</p>	<ul style="list-style-type: none"> <li>✓ Muscle atrophy (caused by ↑ protein catabolic).</li> </ul>	<p>Exophthalmos جحوظ العين</p> 	<ul style="list-style-type: none"> <li>✓ Anxious staring expression.</li> <li>✓ protrusion of eye balls (mostly caused by accumulation of polysaccharides which attract water with it behind the eye balls).</li> </ul> <p>نشوفها في حالات Graves' disease</p> <p>Why &amp; how?</p> <ul style="list-style-type: none"> <li>✓ Polysaccharides accumulates behind the eye &amp; it starts to attract water with it, so they push the eye forward.</li> <li>✓ TSI will also stimulate the accumulation of these polysaccharides.</li> </ul> <p>يعني تتجمع بوليساكارايدز وراء العين وتسحب معاها مويه، تراكمهم راح يدف العين على قدام فيصير جحوظ.</p>
<p>Neurological</p>	<ul style="list-style-type: none"> <li>✓ Tremor.</li> <li>✓ Enhanced reflexes.</li> <li>✓ Irritability Because of hyper excitability of the whole body.</li> </ul>	<p>Others</p>	<ul style="list-style-type: none"> <li>✓ Menstrual cycle disturbance.</li> </ul> <p>(In both hypo &amp; hyper)</p>

# Investigation & Treatment

## ▶ Investigation:



The diagnosis of hyperthyroidism is based on the measurement of T3, T4 and TSH levels.

### A. 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.

### B. In secondary hyperthyroidism:

- ✓ The disorder is in the hypothalamus or anterior pituitary.
- ✓ There will be high level of T4, T3 & TSH.

## ▶ Treatment:

### 1. Medical therapy:

- ▶ By administration of drugs e.g. propylthiouracil, which inhibit the synthesis of thyroid hormones. usually for 12-18 months course with 3-4 monthly monitorin (because it we're working according to the feedback mechanism).

### 2. Surgery: subtotal thyroidectomy.

#### ▶ Indication for surgery:

1. Relapse after medical treatment.
2. Drug intolerance.
3. Cosmetic.
4. Suspected malignancy.

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



# Hypothyroidism

- ▶ Under activity of the thyroid gland.
- ▶ More in women (30-60 years).
- ▶ More common than Hyperthyroidism & very common in Saudi Arabia.
- ▶ Hypothyroidism diagnose is frequently confused with depression.

## How does she look?

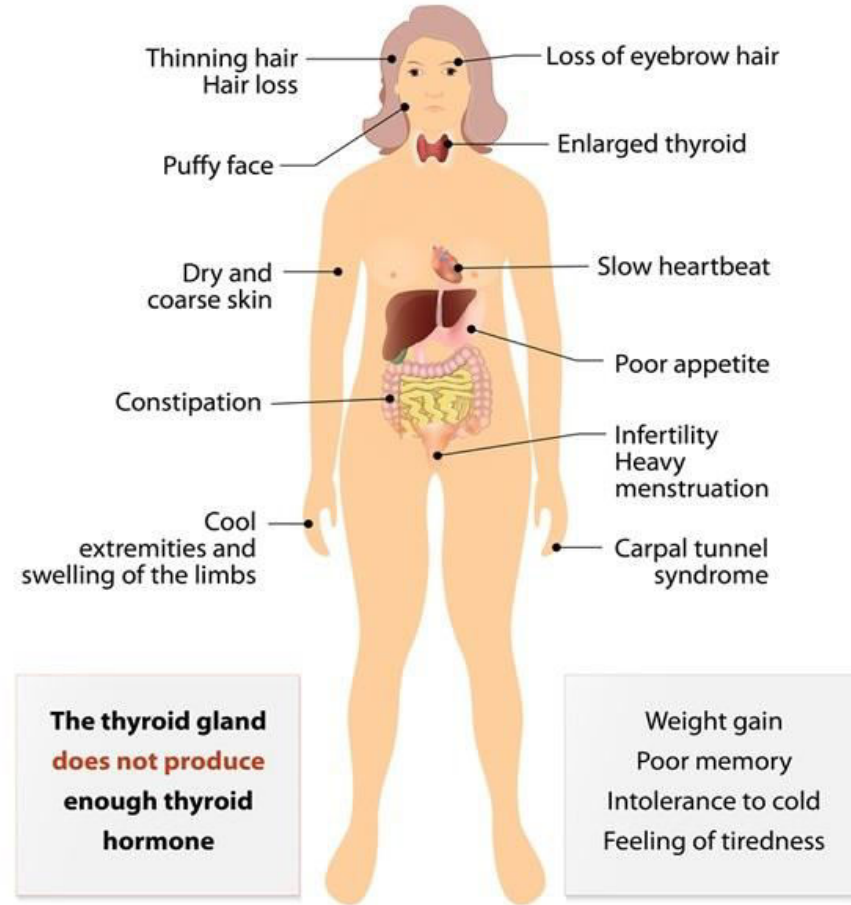
تعبانة، نعسانة، خاملة أغلب الوقت، مكتئبة ومالها خلق شيء

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



مهمة هالصورة لا تنسونها

## Symptoms of HYPOTHYROIDISM



# Causes

## 1. Inherited abnormalities of thyroid hormone synthesis

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

## 2. Endemic Colloid Goiter *يعني محصور في منطقة معينة*

- ▶ Before table salt.
- ▶ Low iodide → low hormone formation → increased TSH → Thyroglobulin → increased size > 10 times.



كانت هذي الحالة منتشرة بشكل كبير قبل وجود ملح الطعام (فيه كمية كبيرة من اليود) اللي عندهم هذا المرض يكون الثايرويد كبير جدا بس ليش حجم الثايرويد كبير جدا؟

- ▶ Because there is No Iodine means no thyroid hormones. No thyroid hormones will result through feedback mechanisms in the increase of TSH.
- ▶ As we know, TSH has two effects, which are increase in secretion and increase in size (trophic effect)
- ▶ In this case, there is no Iodine, thus secretion can't be increased so the only action of TSH will be trophic effect. The body will produce more TSH (because there isn't any thyroid hormones) and all of that TSH will increase the gland's size massively

## 3. Idiopathic Nontoxic Colloid Goiter

- ▶ Iodine intake is normal.
- ▶ Thyroiditis (one of the theories).
- ▶ Inflammation (thyroiditis) → increased cell damage → decreased hormone secretion → increased TSH → increased activity of normal cells → increased size.
- ▶ Idiopathic, one of the theories is inflammation of thyroid (thyroiditis).
- ▶ Inflamed cells won't secrete hormones. If thyroid hormones are deficient, body will synthesize more TSH and will result in increased activity of normal cells and an increase in size.

## 4. Gland destruction (surgery)

مثلاً كان عند المريض هايبر، وسوا له عملية والجراح شال من الغدة أكثر من اللازم

سوا عملياته والجراح شال من الغدة أكثر من اللازم، راح يصير عنده هايبو.

## 5. Pituitary diseases or tumor

- ▶ No TSH


## 6. Hypothalamus diseases or tumor

- ▶ No TRH.

# Diagnosis

تجيك وحده متلحفه بكل الدولاب، خاملة اغلب الوقت، ماتأكل، مالها خلق شيء وسمينه.

## Signs and symptoms

skin	<ul style="list-style-type: none"> <li>✓ Dry skin due to decrease amount of sweat.</li> <li>✓ Cold intolerance (decrease metabolism of the body → decrease production of heat and energy).</li> </ul>	Cardiovascular	<ul style="list-style-type: none"> <li>✓ Decrease in heart rate &amp; stroke &amp; blood volume.</li> </ul>
		G.I tract	<ul style="list-style-type: none"> <li>✓ Constipation.</li> <li>Decrease in appetite &amp; weight gain caused by ↓ BMR “basal metabolic rate”.</li> </ul>
Musculoskeletal	<ul style="list-style-type: none"> <li>✓ ↑ Muscle bulk (decrease in metabolism of proteins which will lead to muscle hypertrophy).</li> <li>✓ ↓ In skeletal growth.</li> <li>The bones will become brittle هشئة why? Because thyroid hormones potentiate the affect of growth hormone. So if the thyroid hormones aren't there the growth hormone won't function.</li> <li>✓ Muscle sluggishness.</li> <li>✓ Slow relaxation after contraction.</li> </ul>	<p>Myxedema</p> 	<ul style="list-style-type: none"> <li>✓ An emergency.</li> <li>✓ An edematous appearance through out the body.</li> </ul>
		Renal function	<ul style="list-style-type: none"> <li>✓ Decrease glomerular filtration rate.</li> </ul>
Neurological 😊 لا تشكون بنفسكم	<ul style="list-style-type: none"> <li>✓ Slow movement.</li> <li>✓ Impaired memory.</li> <li>✓ Decrease mental capacity.</li> </ul>	Others	<ul style="list-style-type: none"> <li>✓ Loss of libido (loss the sense of sexual drive).</li> <li>✓ Menstrual cycle disturbance (in both hyper &amp; hypo).</li> </ul>

# Investigation & Treatment

## ▶ Investigation:

The diagnosis of hyperthyroidism is based on the measurement Serum T3,T4, (low).

### A. TSH is elevated in primary:

- ▶ The disorder is in the thyroid gland.
- ▶ There is low amount of T3 and T4 secreted, so the pituitary thinks that its not secreting enough TSH, so it will increase the secretion of TSH.

### B. TSH is low in secondary hypothyroidism:

- ▶ The disorder is in the hypothalamus or anterior pituitary.
- ▶ There will be low TSH, so there will be low T3 & T4 also.

## ▶ Treatment:

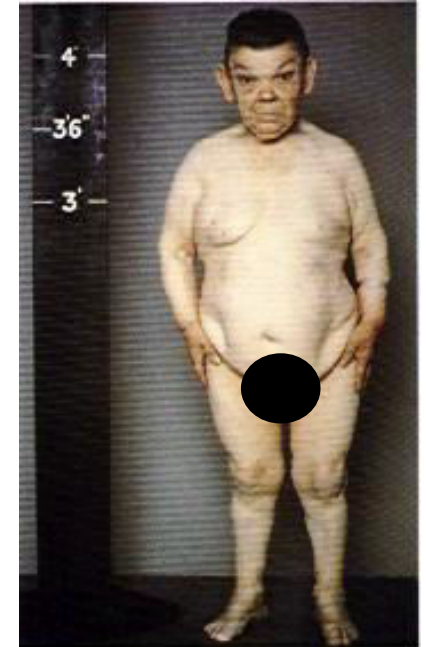
L-thyroxine (Hormone replacement therapy, MUST monitor & adjust dose).

- ✓ Starting dose is 25-50 µg.
- ✓ Increase to 200 µg.
- ✓ At 2-4 weeks period.
- ✓ The first response seen is the weight loss.

# Cretinism



Cretinism التقرم			
Definition	Causes	Symptoms	Treatment
<p>Extreme <b>hypothyroidism</b> during infancy and childhood (failure of growth).</p> <p>(Inability to secrete the thyroid hormone. Thyroid hormone isn't there).</p>	<p>1. Congenital lack of thyroid gland. <b>(Congenital Cretinism).</b></p> <p>2. Genetic deficiency leading to failure in production of hormone.</p> <p>3. Iodine lack in the diet. <b>(Endemic Cretinism).</b></p>	<ol style="list-style-type: none"> <li>1. Infant appears normal at birth but abnormality appears within weeks.</li> <li>2. Protruding tongue (tongue sticks out).</li> <li>3. Dwarf with short limbs.</li> <li>4. Mental retardation.</li> <li>5. Often the infant is present with <b>Umbilical Hernia.</b></li> <li>6. Delayed eruption of teeth.</li> </ol>	<p>Changes are irreversible unless if treatment is given early.</p>



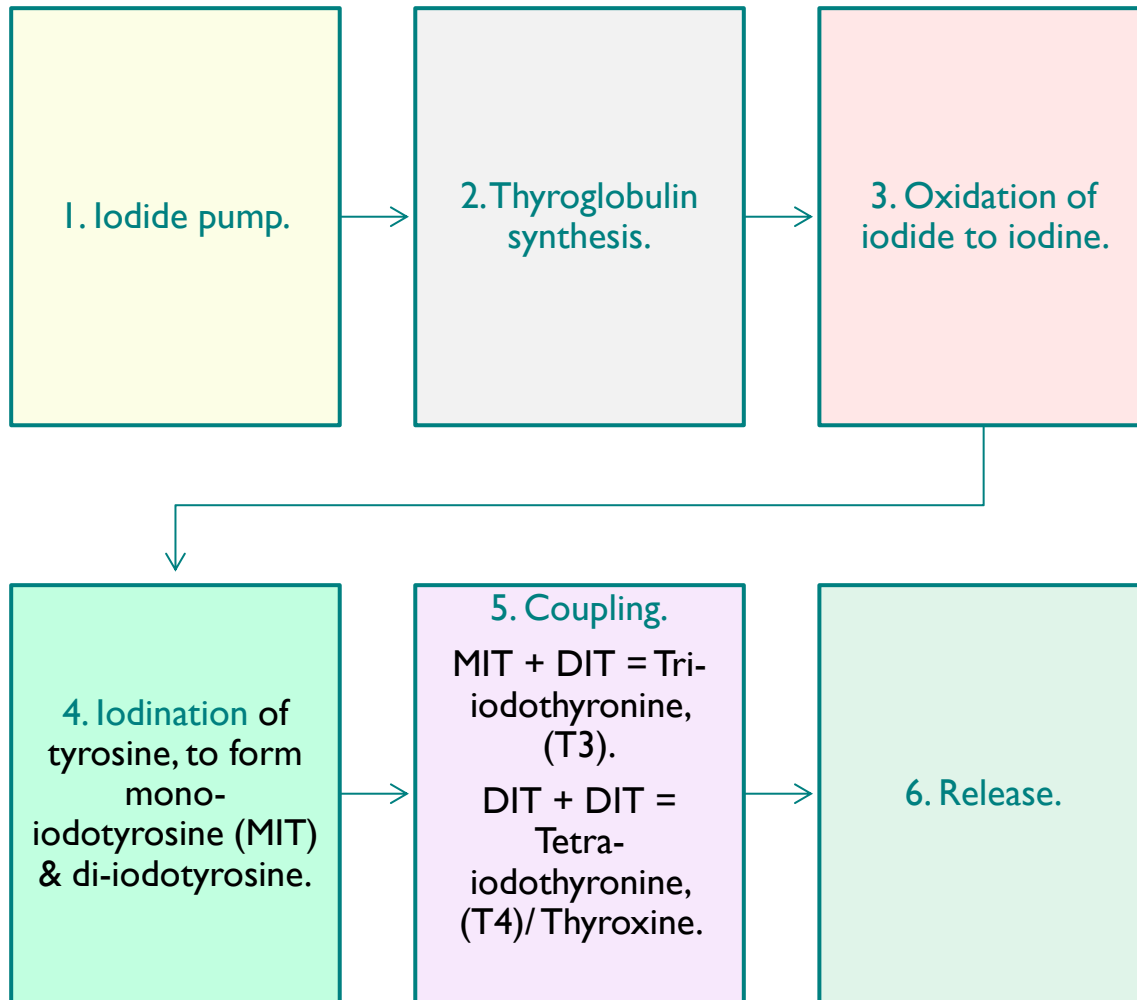
Umbilical Hernia



Protruding tongue



# Summary of steps in biosynthesis of thyroid hormones (From slides)



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

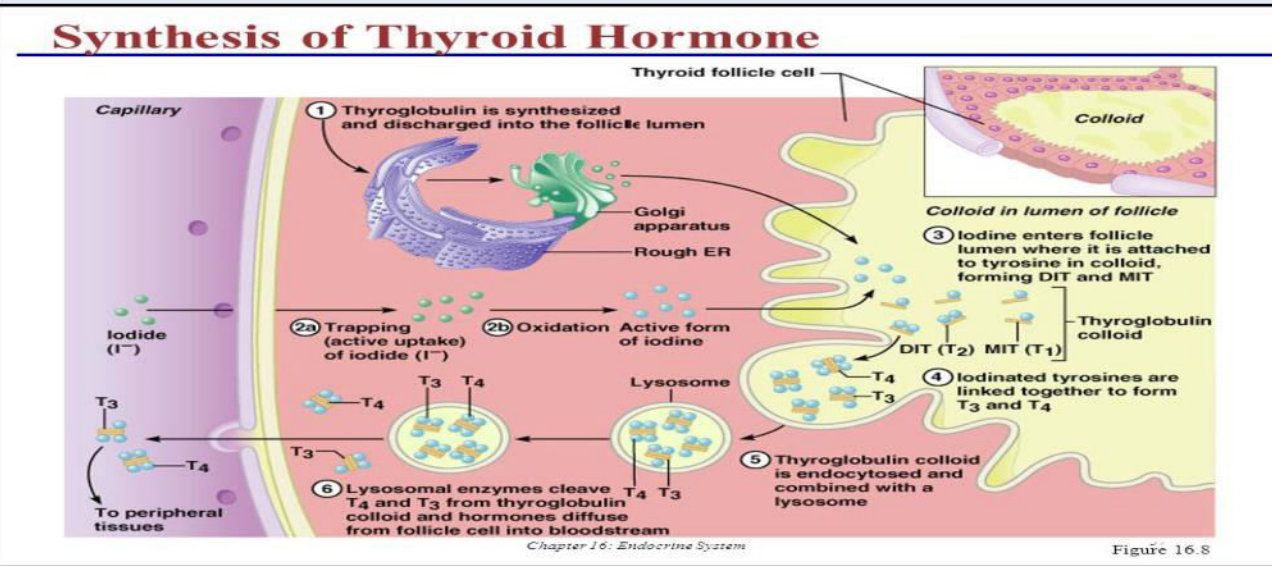
Copyright © 2010 by Saunders, an imprint of Elsevier Inc. All rights reserved.

# Summary

Hormones	Thyroid Hormones in the circulation	Thyroid Hormones Actions	Diseases of Thyroid Gland		
<ul style="list-style-type: none"> <li>○ <b>T4</b> } Synthesized in Follicular cells</li> <li>○ <b>T3</b> } Some of T4 is converted into rT3</li> <li>○ <b>rT3</b> } (inactive form of T3)</li> <li>○ <b>Calcitonin</b> (Synthesized in the parafollicular cells)</li> </ul>	<ul style="list-style-type: none"> <li>○ Bound (TBG and albumin)</li> <li>○ Unbound (less in number)</li> </ul>	<ul style="list-style-type: none"> <li>○ Growth: Growth formation and bone maturation</li> <li>○ CNS: Maturation of CNS</li> <li>○ BMR: ↑Na-K ATPase, ↑O<sub>2</sub> consumption, ↑Heat production and ↑ BMR</li> <li>○ Metabolism: Increased</li> <li>○ Cardiovascular: Increased.</li> </ul>	<b>Hyperthyroidism</b>	<b>Hypothyroidism</b>	<b>Cretinism</b>
<p><b>Liver and Pregnancy</b></p> <ul style="list-style-type: none"> <li>✓ In liver diseases, TBG becomes low hence increased FREE T3/T4 which inhibits Thyroid secretion</li> <li>✓ During pregnancy, high estrogen increases TBG hence low FREE T3\4 which stimulates Thyroid.</li> </ul>			Over activity of the gland. Graves' disease. Weight loss, heat intolerance.	Under activity of thyroid gland. Endemic Colloid Goiter. Weight gain, cold intolerance.	Extreme hypothyroidism during infancy and childhood. Protruding tongue, mental retardation and umbilical hernia.

Enzymes&Stimulation!	Regulation of thyroid secretion	Biosynthesis of thyroid Hormones
----------------------	---------------------------------	----------------------------------

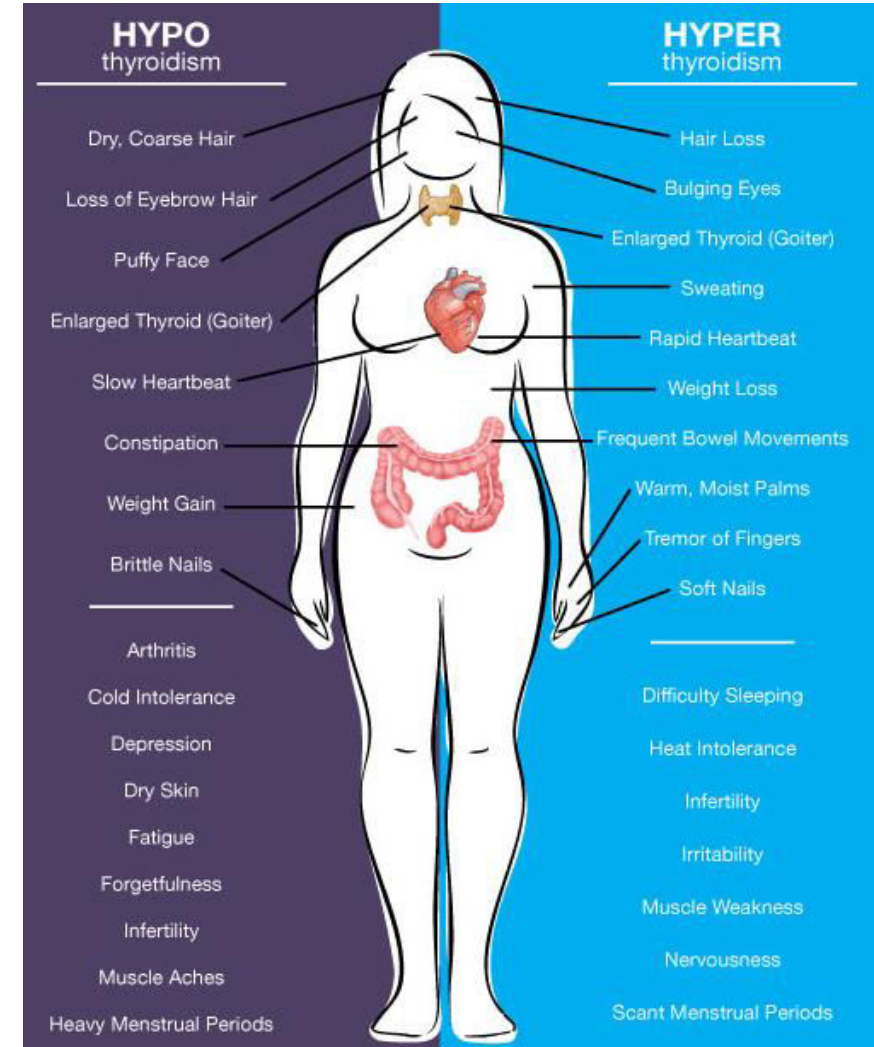
<ul style="list-style-type: none"> <li>○ <b>TSH stimulates the active transport of Iodide</b></li> <li>○ <b>Thyroid peroxidase</b> (Oxidation of Iodide to Iodine, Organification of Thyroglobulin and coupling of DIT and MIT)</li> <li>○ <b>Thyroid deiodinase</b> (Deiodination of DIT and MIT)</li> <li>○ <b>Iodinase enzyme</b> (Deionization of T4 to T3)</li> </ul>	<ul style="list-style-type: none"> <li>○ It is regulated by the <b>HYPOTHALAMIC-PITUITARY AXIS</b></li> <li>○ Two hormones are released within this axis; <b>TRH and TSH</b></li> <li>○ There are other stimulatory and inhibitory factors affect Thyroid hormone secretion such as Thyroid stimulating immunoglobulins and Iodide imbalance</li> </ul>
--	---



# Summary of hypo-hyperthyroidism

	Hyperthyroidism	Hypothyroidism
Definition	Over activity of the thyroid gland; Increase in secretion + increase in size.	Under activity of the thyroid gland
More common in women		
Causes	<ol style="list-style-type: none"> <li>Graves' disease: common cause</li> <li>Autoimmune disorder; ↑ circulating level of (TSIs).</li> <li>Thyroid gland tumor</li> <li>Exogenous T3 and T4</li> <li>Excess TSH secretion</li> <li>Diseases of the pituitary and hypothalamus.</li> </ol>	<ol style="list-style-type: none"> <li>inherited abnormalities of thyroid hormone synthesis Peroxidase defect, Iodide trapping defect, Thyroglobulin defect.</li> <li>Endemic Colloid Goiter</li> <li>Idiopathic Nontoxic Colloid Goiter: Thyroiditis</li> <li>Gland destruction (surgery).</li> <li>Pituitary diseases or tumor.</li> <li>Hypothalamus diseases or tumor.</li> </ol>
Symptoms	<ol style="list-style-type: none"> <li>Goiter in 95%.</li> <li>Heat intolerance, night sweating, smooth, warm and moist skin.</li> <li>Muscle atrophy</li> <li>Tremor, enhanced reflexes, irritability.</li> <li>↑ HR and stroke volume, arrhythmias, hypertension.</li> <li>Weight loss and Diarrhea.</li> <li>↑ Glomerular filtration rate</li> <li>Menstrual cycle disturbance</li> <li>Exophthalmos</li> </ol>	<ol style="list-style-type: none"> <li>Myxoedema</li> <li>Cold intolerance, dry skin.</li> <li>↑ Muscle bulk, ↓ In skeletal growth, muscle sluggishness.</li> <li>Slow movement, impaired memory, ↓ mental capacity.</li> <li>↓ Blood volume, ↓ HR and stroke volume.</li> <li>Increase weight and Constipation</li> <li>↓ Glomerular filtration rate</li> <li>Menstrual cycle disturbance.</li> </ol>
Investigation	Serum TSH, T4 and T3 measurement: <ul style="list-style-type: none"> <li>In <b>primary</b> hyperthyroidism: ↑ T3, T4 and ↓ TSH.</li> <li>In <b>secondary</b> hyperthyroidism: ↑ T3, T4 and ↑ TSH.</li> </ul>	Serum TSH, T4 and T3 measurement: <ul style="list-style-type: none"> <li>T3, T4 are ↓</li> <li>TSH ↑ in <b>primary</b> BUT ↓ <b>secondary</b> hypothyroidism</li> </ul>
Treatment	<ol style="list-style-type: none"> <li>Medical therapy: e.g. Propylthiouracil</li> <li>Surgery: thyroidectomy</li> </ol>	<ol style="list-style-type: none"> <li>Thyroid hormone replacement therapy e.g. L- thyroxine</li> </ol>

❖ **CRETINISM: Extreme hypothyroidism during infancy and childhood (failure of growth).**



# Thank you for checking our work!



اعمل لترسم بسمة، اعمل لتمسح دموعه، اعمل و أنت تعلم أن الله لا يضيع أجر من أحسن عملا.

قادة الفريق:

ليلى مذكور & محمد

خالص الشكر لأعضاء الفريق الكرام:

أسيل بادخن

عبدالرحمن الراشد

باسل المفلح

حنين باشيخ

عبدالعزيز العنقري

حسان الشمري

دعاء عبدالفتاح

عبداللطيف عبداللطيف

حمد الخضيرى

دعاء ماهر

فارس الجعفر

خالد القحطاني

زينة الكاف

قيس المهيدب

طلال الحقيلى

نوف العمارى

نواف الخضيرى

عبدالله السعيد



Please check our editing file to know if there are any additions, changes or corrections.



Examine yourself



2017-2018 Dr. Nervana Bayumi's Lecture & Notes.  
2017-2018 Prof. Abdulmajeed Aldress's Lecture & Notes.  
Guyton & Hall of Medical Physiology 13th Edition.  
Linda S. Costanzo 5th Edition.



Helpful physiology books.



Give us your feedback 😊