Thyroid Disorders

Objectives:

- **How to evaluate a patient with thyroid disease**
- **Hypothyroidism and hyperthyroidism**
  - **Causes**
  - **pathogenesis**
  - **diagnosis**
  - **treatment**
- **Other thyroid disorders**

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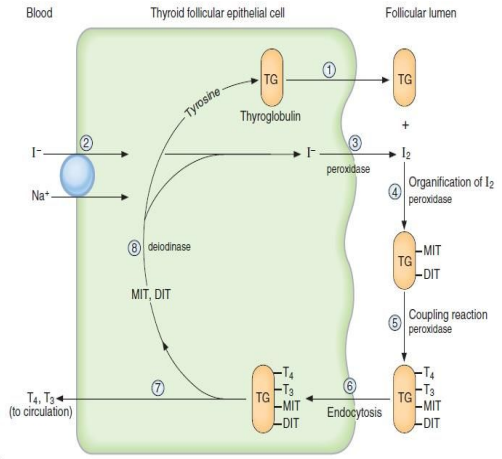
- Editing file
- Feedback

Basic Review of Thyroid Gland

★ Recall synthesis of thyroid hormones (or don't)

1. Endoplasmic reticulum synthesizes thyroglobulin (contains tyrosine), Golgi apparatus packages and sends the thyroglobulin to the colloid.
2. In the basolateral surface, iodide(-) is picked up from blood and trapped into the follicular cell via NIS (sodium-iodine-symporter).
3. On the apical surface, (Pendin) transporter transports iodide into the colloid, in the colloid iodide(-) is oxidized into iodine via Thyroid Peroxidase.
4. Now iodine will bind to the Tyrosine ring on the thyroglobulin. When;
5. One iodine binds to tyrosine --> MIT (monoiodotyrosine)
6. Two iodine bind to tyrosine --> DIT (diiodotyrosine)
7. After that, MIT & DIT or DIT & DIT can form bonds with each other;
8. MIT + DIT = T3 (Triiodothyronine)
9. DIT + DIT = T4 (Thyroxine)
10. Not done yet -_- because T3 & T4 are still attached to the thyroglobulin. The compound gets endocytosed back into the follicular cell. Then it combines with a lysosome to hydrolyze the peptide chain & release the thyroid hormones (T3& T4).
11. T4 & T3 are sent to the circulation bounded to thyroid binding proteins (Thyroxine binding globulin TBG). (Because they're lipid hormones)



Note that:

- T4 is more secreted from the thyroid than T3.
- However T3 is 5x more active than T4.
- Once reaching the target cells T4 is converted to T3 via iodinase enzyme.
- Because thyroid hormones are lipid soluble, they enter the nucleus of target cells to initiate their actions.

★ Physiological effects of thyroid hormones:

Target Tissue	Effect	Mechanism
Heart	Chronotropic	Increase number and affinity of beta-adrenergic receptors.
	Inotropic	Enhance responses to circulating catecholamines. Increase proportion of alpha myosin heavy chain (with higher ATPase activity).
Adipose tissue	Catabolic	Stimulate lipolysis.
Muscle	Catabolic	Increase protein breakdown.
Bone	Developmental	Promote normal growth and skeletal development.
Nervous system	Developmental	Promote normal brain development.
Gut	Metabolic	Increase rate of carbohydrate absorption.
Lipoprotein	Metabolic	Stimulate formation of LDL receptors.
Other	Calorigenic	Stimulate oxygen consumption by metabolically active tissues (exceptions: adult brain, testes, uterus, lymph nodes, spleen, anterior pituitary). Increase metabolic rate.

Hyperthyroidism and thyrotoxicosis

- **Hyperthyroidism:** hyperactivity of the thyroid gland **.** Overproduction (increase synthesis and release) of thyroid hormone, due to primary (thyroid itself) or secondary (pituitary) cause.
- **Thyrotoxicosis:** is the clinical syndrome that results when tissues are exposed to high levels of circulating thyroid hormone . is a metabolic state caused by elevated circulating FT4 & FT3

★ Conditions Associated with thyrotoxicosis :

- Diffuse toxic goiter (Grave's disease) most common
- Toxic Adenoma
- Toxic multinodular goiter
- Subacute Thyroiditis 2nd most common. initially causes hyper then hypo.
- Hyperthyroid phase of hashimoto's thyroiditis
- Thyrotoxicosis factitia thyroxine ingested to decrease weight
- Rare:Ovarian struma , metastatic thyroid carcinoma (follicular) , hydatidiform mole , TSH secreting pituitary tumor , pituitary resistance to T3 and T4 .

★ Diffuse toxic goiter (Grave's disease) we will focus on this mainly : watch!

- Most common form of thyrotoxicosis
- females > males
- Features :
  - ❏ thyrotoxicosis
  - ❏ goiter
  - ❏ orbitopathy(Exophthalmos)
  - ❏ dermopathy(pretibial myxedema)
  - ❏ thyrotoxicosis + exophthalmos = graves disease

★ Etiology:

- Most common cause of hyperthyroidism (up to 80% of all cases of hyperthyroidism).
- Autoimmune disease of unknown cause .
-peak incidence in the 20 to 40 year age group .

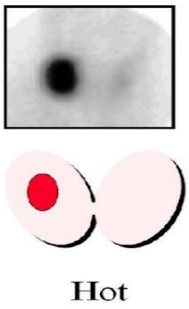
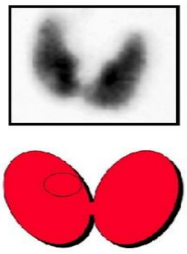
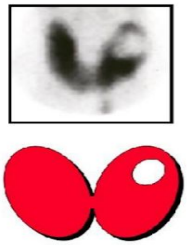
➔ **Pathophysiology:** The thyrotoxicosis in Grave's disease results from the production of IgG antibodies directed against the TSH receptor (TSH receptor antibodies, TSH stimulating antibodies), stimulation of TSH receptor on the thyroid follicular cells increases thyroid hormone production & cell proliferation (Diffuse goiter in most cases).but we can't control it . unlike the TSH released from the pituitary .

➔ **Pathogenesis:** Local viral infection → inflammatory reaction leading to the production of IFN-g and other cytokines by non-thyroid-specific infiltrating immune cells → will induce the expression of HLA class II molecules on the surface of thyroid follicular cells.→ Subsequently, thyroid specific T-cells will recognize the antigen presented on the HLA class II molecules and will be activated →The activated thyroid-specific T-cells stimulate B cells to produce → TSH receptor-stimulating antibodies → hyperthyroidism

★ thyroid function test:

Hyperthyroidism			
Types	**Clinical Hyperthyroidism**	**Subclinical Hyperthyroidism**	**TSH Mediated Hyperthyroidism** Secondary hypothyroidism
Blood Test	-FT4 high -FT3 high -TSH low -you can make the diagnosis by TSH alone , but we do T4 to make sure the grade of graves isn't really severe . ❑ If there is Eye signs exophthalmus : No further tests ❑ If there is No eye signs : Do thyroid scan	FT4 normal FT3 normal (upper borderline!) TSH low the pituitary is sensing the overproduction of thyroid hormones so TSH decreases before the level T3, T4 get high	FT4 high FT3 high **TSH high** TSH secreting tumor (not responding to - feedback)

★ Thyroid Scan غالبًا لمّا نلقى زيادة بالثايروید هورمون وما كان التشخيص واضح اكلينيكيًا, الخطوة الثانية إننا نطلب
Radioiodine uptake test

	Hot: low risk of malignancy.	Warm: low risk of malignancy.	Cold:Higher risk of malignancy (although most cold nodules are benign).
	 Hot ❖ **Examples :** -Grave's disease -TMN	 Warm	 Cold ❖ **Examples :** -Spontaneous resolving hyperthyroidism -Subacute Thyroiditis , inflammation the gland is destroyed , so low uptake -Thyrotoxic phase of hashimoto's thyroiditis -Iodine loaded patients -Patients on LT4 therapy -Struma ovarii

- Nodules detected by thyroid scans are classified as cold, hot, or warm. If a nodule is composed of cells that do not make thyroid hormone (don't absorb iodine), then it will appear "cold". A nodule that is producing too much hormone will show up darker and is called "hot." If appearing "warm" it's producing normal amount of hormones.

★ Symptoms

Clinical Manifestation Of Hyperthyroidism (↑ Thyroxine)	
skin	sweating , moist , thin hair .
Brain	Hyperthermia, Heat intolerance, Increase appetite, Anxiety, Hand tremor
GIT	Hyperdefecation, Loose bowel motion, Increase gluconeogenesis (Failure of controlling a known DM)
Renal	Urinary frequency
Heart	Palpitation, Sinus tachycardia, Atrial fibrillation
Eye	Eyelid lag, Eyelid retraction (staring gaze) Why? because thyroid hormones potentiate the effect of sympathetic innervation on the eyelid muscle (levator palpebra) → contraction.
Bone	Bone fracture, Osteoporosis, Hypercalcemia
Muscles	Muscle wasting & weakness, Hyperreflexia, Weight loss
Reproductive	Female: Menstrual cycles disturbances (Oligo-or amenorrhea)/ Male: ED

★ Diagnosis

Diagnostic approach of Hyperthyroidism	
Clinically	- **Atypical presentations:** ● Thyrotoxic periodic paralysis (most common in asians , they present with changes in electrolyte and hypokalemia) ● Thyrocardiac disease ● Apathetic hyperthyroidism (in elderly , they present with weight loss only)Symptoms of hyperthyroidism are blunted in elderly people. they don't present with ideal symptoms of hyperthyroidism. some present with only depression, Afib, CHF, or weakness. وممكن المريض يجيك خالي من التعابير ، تقوله نكتة ما يضحك. ● Familial dysalbuminemic hyperthyroxinemia rare
Biochemically	-TSH-R Ab (Stim) it increases in graves' disease -Free T3 in T3 toxicosis when T4 is normal

★ Complications:

Thyrotoxic crisis (thyroid storm) :

- Predisposing conditions

Clinical features:

- Fever / Agitation they can't sit in the bed , very agitated !
- Altered mental status
- Atrial fibrillation / Heart failure

★ Treatment of graves' disease

A. Antithyroid drug therapy : in severe graves' disease you can only use meds! to decrease the level of the gland to a level that you can deal with it

- ❑ **Propylthiouracil "is safe for pregnant ladies" or methimazole**

-Spontaneous remission 20-40%
-Relapse 50-60%
-Duration of treatment 6 months years
-Reactions to antithyroid drugs rare

- ❑ **b-blockers** to treat symptoms
- ❑ **SSKI** Super saturated pottasium Iodine , it decreases synthesis of thyroid hormones

B. Surgical treatment: If meds and radioactive iodine failed

-Subtotal thyroidectomy
-Preparation for surgery control his HR,BP, thyroxine levels
-Complications:
* hypothyroidism/ hypoparathyroidism and hypocalcemia
* Recurrent laryngeal nerve injury hoarseness

C. Radioactive iodine therapy: most common therapy . If you have exophthalmos its contraindicated because it makes it worse .

- I^{131} is most commonly used
-Dose:

$$\frac{I^{131}\text{ (uci/g) x thyroid weight}}{\text{24-hr RAI uptake}} \times 100$$

- **Treatment of Graves' disease <u>complications</u>**:

-Thyrotoxic crisis with high dose you need to first prevent the conversion of T4 to T3 with steroids then you give propylthiouracil then you give IV fluid Beta blockers and Iodine.
- Orbitopathy refer to ophthalmologist / give eye drops
- Thyrotoxicosis and pregnancy some meds. affect the baby

- **Treatment of <u>other forms of thyrotoxicosis:</u>**

-Toxic adenoma if the thyroid has an adenoma producing thyroxine :
1)Meds 2)radio-Iodine(if it's small) 3)surgery (preferably if it's big)
-TMN toxic multinodular goiter , same approach .
-Amiodarone
-Subacute thyroiditis you have to differentiate it from graves because the treatment is different . here you only treat symptomatically until the inflammation subsides .
-Thyrotoxicosis factitia take good history
-Struma ovarii

- how to treat exophthalmos?
  1- if active > steroids
  2- inactive > Refer to ophthalmology for decompression.

- if someone is taking Amiodarone and developed hyperthyroidism, Do not stop the medication! you should treat the complications. treatment depend on the type of hyperthyroidism he developed:
  1- if graves type → treat with anti-thyroid.
  2- if thyroiditis type → symptomatic treatment (Beta-blockers, Aspirin, paracetamol)
- If i ask you how to treat toxic adenoma or toxic multinodular goitre, is it by medication, surgery
- or RAI ? you should answer ALL. medications to start with, then surgery or RAI

Hypothyroidism Watch!

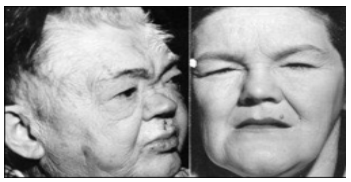
Etiology of hypothyroidism

Primary causes	Secondary causes	Tertiary causes
primary = source of problem = thyroid itself ❑ Hashimoto's Thyroiditis: most common cause recently , before it was iodine deficiency . characterized by formation of antibodies against Thyroglobulin (thyroid hormone precursor) and Thyroid peroxidase (important thyroid enzyme) destructive lymphoid infiltration of the thyroid, ultimately leading to a varying degree of fibrosis and thyroid enlargement. (Diffuse goiter) -with goiter No iodide > No Thyroid Hormones (T4, T3) > Increase release TSH > Goiter -"Idiopathic" thyroid atrophy , presumably end-stage autoimmune disease , following either Hashimoto's thyroiditis or graves disease . -Neonatal hypothyroidism due to placental transmission of TSH-R blocking antibodies . ❑ Radioactive iodine therapy for graves' disease it causes destruction of the gland . ❑ Subtotal thyroidectomy for graves' or nodular goiter 2nd most common ❑ Excessive iodine intake (Kelp , radiocontrast dyes) ❑ Subacute thyroiditis its an inflammatory process that is caused by viruses or chemicals … ❑ Iodide deficiency ❑ Other goitrogens such as lithium , amiodarone , antithyroid drug therapy . ❑ inborn errors of thyroid hormone synthesis , that's why for the last 5 years they screen all infants for TSH .	-(MCQs) Secondary = Source of problem = pituitary -Pituitary → decreased TSH → decreased thyroid hormones ❑ Hypopituitarism due to: - Pituitary adenoma - pituitary ablative therapy - pituitary destruction	❑ Hypothalamic dysfunction rare . TRH will be low

other causes:

peripheral resistance of the action of thyroid hormones :
mutation in thyroid hormone receptors in cells leading to High hormones in blood but symptoms of hypothyroidism

★ Pathogenesis:

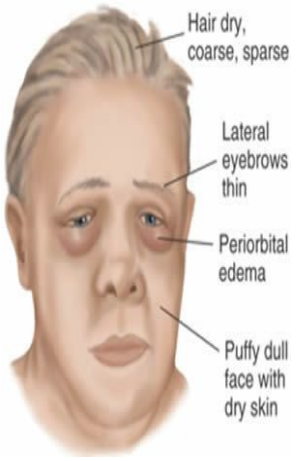


- Thyroid hormone deficiency affects every tissue in the body, so that the symptoms are multiple
- Accumulation of glycosaminoglycans-mostly hyaluronic acid in interstitial tissues (accumulation causes edema in the face , heart which causes pericardial effusion , hands which causes carpal tunnel syndrome because of compression on the nerves)
- Increase capillary permeability to albumin
- Interstitial edema can affect any part of the body (skin, heart muscle, striated muscle)
  - Why does edema happen in hypothyroidism ?because TSH becomes high and that stimulates fibroblasts to increase the deposition of glycosaminoglycan , which results in osmotic edema

★ Clinical Features:

- Common feature: easy fatigability, coldness, weight gain, constipation, menstrual irregularities, and muscle cramps. common symptoms and can be associated with any disease (not specific nor sensitive).
- Physical findings: cool rough dry skin, puffy face and hands, hoarse husky voice, and slow reflexes, yellowish skin discoloration.

Clinical Manifestation of Hypothyroidism DECREASE FUNCTIONS OF THE ORGANS "except menstrual flow"	
Anemia **why?** the gut has a problem in absorption because of edema	• Impaired Hb synthesis • Iron deficiency • folate deficiency • pernicious anemia , with B12 deficient megaloblastic anemia.
skin	• Scaliness of skin, Brittle hair and loss of outer eyebrow
Pulmonary	• Shallow and slow respiration • respiratory failure
GIT	• Chronic Constipation • Ileus • malabsorption
Renal	• Impaired GFR Significantly decreased but when you treat Cr. level returns to normal . • Water intoxication
CNS	• Chronic fatigue • lethargy • decreased concentration • Anovulatory cycles and infertility • depression • agitation • memory loss
Heart	• Bradycardia • Decreased cardiac output Low voltage ECG (because of pericardial effusion , so the signals won't reach the electrodes) • Cardiomegaly • Pericardial effusion
NeuroMuscular	• Proximal Myopathy • Delayed Relaxation Reflexes • Severe muscle cramps • Paresthesias • Muscle weakness • Carpal tunnel syndrome
Reproductive	• Male → Loss of libido. • Women → Menorrhagia.



- **Hypothyroidism patients are prone to develop Atherosclerosis. Why?**Because lack of Thyroid hormone → decrease liver uptake of LDL and decrease secretion of cholesterol in bile → Increase blood cholesterol → Atherosclerosis

★ Complications

1- Regarding **myxedema coma** :

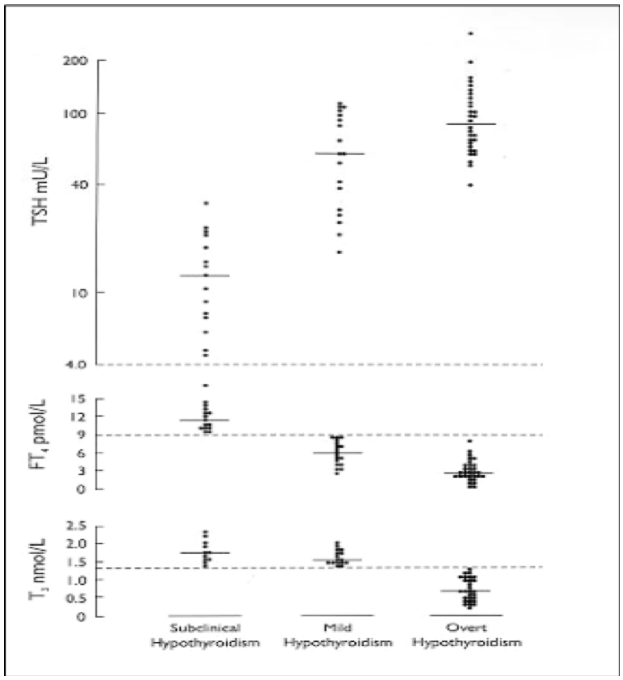
- ➔ The end-stage of untreated hypothyroidism
- ➔ Progressive weakness , stupor , hypothermia , hypoventilation , hypoglycemia , hyponatremia , water intoxication , shock , and death .
- ➔ Associate illness and precipitating factors : pneumonia , MI , cerebral thrombosis , GI bleeding , ileus , excessive fluid administration , and administration of sedatives and narcotics .
- ➔ Three main issues : CO2 retention and hypoxia , fluid and electrolyte imbalance and hypothermia

2- **Myxedema and heart disease**.(patient with heart disease on levothyroxine treatment can get heart problems , because he has low metabolism then sudden increase in the metabolism happens so the heart can get ischemic)

3- **Hypothyroidism and neuropsychiatric disease.** you can't trust that he is going to take the meds. as prescribed .

★ Diagnosis:

Hypothyroidism		
Biochemical	**TRH stimulation test** **Not used anymore**	**Serology** **Thyroid Ab**
- Primary Hypothyroidism:High TSH, Low T4. T3 is only important in Hyperthyroidism when we suspect T3 thyrotoxicosis. - Secondary Hypothyroidism: Low TSH, Low T4 - If I had to choose one test I will choose TSH because it is the most important test used to diagnose primary hypothyroidism. we order free T4 if we suspect secondary hypothyroidism.So basically we first order TSH if it's high then it's hypothyroidism for sure . if it was normal or low , we order T4 to check for secondary hypothyroidism .	The **TRH test** involves administration of a small amount of **TRH** intravenously, following which levels of TSH will be measured at several subsequent time points using samples of blood taken from a peripheral vein. The **test** is used in the differential diagnosis of secondary and tertiary hypothyroidism.	- Thyroid Peroxidase autoantibodies. - Anti-Thyroglobulin Antibodies. - we order thyroid AB if we suspect autoimmune thyroid disease. - we can have autoimmune thyroid disorder with normal thyroid Antibodies , it's not 100% specific . - Required if the patient has mildly elevated TSH with normal T4.



- individual and median values of thyroid function tests in patients with various grades of hypothyroidism. Discontinuous horizontal lines represent upper limit (TSH) and lower limit (FT4,T3) of the normal reference ranges. Reproduced with permission from Ord WM: On myxedema, a term proposed to be applied to an essential condition in the "cretinoid" affection occasionally observed in middle-aged women. Medico-Chir Trans 1878; 61: 57.

- Subclinical Hypothyroidism: High TSH with normal T4 and T3.
- Mild Hypothyroidism: High TSH with low T3 and normal T4.
- Overt Hypothyroidism: High TSH with low T3 and T4.
- Why are the T3 and T4 is normal in the blood?

to protect the tissue (heart, liver, and brain) there is an enzyme that converts T4 to T3 in the tissue level just to preserve the function to the important organs.

★ Treatment:

A- Levothyroxine (T4).

- ❑ Follow serum Free T4 and TSH. T3 is rarely used.
- ❑ Take dose in AM
- ❑ Do blood test fasting before taking the daily dose
- ❑ Adults: 1.7 ug/kg/d, but lower in elderly (1.6 ug/kg/d) in the elderly start with small doses and increase the dose every two weeks and do a Thyroid Function Test.
- ❑ For TSH suppression (nodular goiters or cancer): 2.2 ug/kg/d
- ❑ Increase dose of T4 in malabsorptive states or concurrent administration of aluminum preparations, cholestyramine, calcium, or iron compounds
- ❑ Increase dose of T4 in pregnancy and lactation
- ❑ The t1/2 of levothyroxine is 7 days.
- ❑ we need 6 weeks to follow up thyroid function test because the t1/2 of thyroxine is 7 days.
- ❑ Scenario : patient diagnosed with primary hypothyroidism you give her thyroxine , she follows up after 6 months and the TSH was high , how will you approach her? first you have to ask if the patient is taking her drugs properly “Compliance” then look for malabsorption state or pregnancy in order to increase the dose.
- ❑ If the patient takes any medications that affects thyroxine absorption , you have to seperate them by 4 hours .

B- Myxedema coma first stabilize the pt.

- ❑ Acute medical emergency
- ❑ Monitor blood gases
- ❑ Patient may need intubation and mechanical ventilation
- ❑ Treat associated medical problems
- ❑ Avoid excessive hydration
- ❑ Assess adrenal function and treat if needed
- ❑ In pituitary myxedema, glucocorticoid replacement is essential
- ❑ IV levothyroxine: loading 300-400 ug, daily maintenance 50 ug
- ❑ Be cautious in patients with coronary artery disease they may develop MI .

- ❑ Active rewarming of the body in contraindicated. we use passive rewarming with blankets , because if we use active rewarming(we will drop the vascular resistant abruptly) and it will induce vasodilation and cause hypotension .
- ❑ confirm from the history of the patient + symptoms . ask the family , friends about compliance of meds. is he out of meds.? is he skipping doses ?

C- Myxedema with heart disease

- ❑ Start treatment slowly in long standing hypothyroidism and in elderly patients particularly those with known cardiovascular disease gradually !
- ❑ 25 ug/d x 2 weeks, increase by 25 ug every 2 weeks until a daily dose of 100-125 ug is reached.

- **Toxic effects of levothyroxine therapy** thyroxine is the safest drug that you will come upon in medical practice

- ❑ No allergy has been reported to pure levothyroxine -
- ❑ If FT4 and TSH are followed and T4 dose is adjusted, no side effects are reported
- ❑ If FT4 is higher than normal if he is talking a higher dose than he needs : hyperthyroidism symptoms may occur
  -Cardiac symptoms
  -Osteopenia and osteoporosis

- **Recommendations for the treatment of myxedema coma**

• hypothyroidism	large initial intravenous dose of 300-500 µg T4; if no response within 48 hours, add T3
• hypocortisolemia	intravenous hydrocortisone 200-400 mg daily
• hypoventilation	don't delay intubation and mechanical ventilation too long
• hypothermia	blankets, no active rewarming: Giving the patient warm saline by an NGT or a catheter.
• hyponatremia	mild fluid restriction
• hypotension	cautious volume expansion with crystalloid or whole blood
• hypoglycemia	glucose administration
• precipitating event	identification and elimination by specific treatment (liberal use of antibiotics)

★ Other Thyroid disorders :

- Nontoxic goiter
- Subacute thyroiditis(De quervains)
- Chronic thyroiditis
- Acute Thyroiditis
- Thyroid nodules
- Thyroid cancer

Hx & Physical Exam of Thyroid

History	1. lithium carbonate for psychiatric pts. It causes hypothyroidism mainly 2. Iodide -is a substrate that is used by thyroid gland to produce hormones- ingestion (Kelp seaweeds that contains iodine, Iodide-containing cough preparation in pts who have chronic cough , Iv iodide-containing contrast Ask if the pt. had a recent cath for example. Can cause both hypo and hyperthyroidism. 3. Residence in an area of low dietary Iodide 4. Radiation exposure it can cause thyroid cancer . Ask if they work in labs , Or if they had many CT scans . Also, if they ever come upon a disaster that causes leak of radioactive material . 5. family history -Thyroid disorders -Immunologic disorders(DM , rheumatoid , pernicious anemia , alopecia,vitiligo,myasethenia gravis , MEN2a)
Examination Do general examination for the whole body	1. Observe the neck , especially as the patient swallows . 2. Examine from the front , rotating the gland slightly with one thumb while palpating the other lobe with the other thumb . 3. Examine from behind , using three fingers and the same technique 4. determine the size of the thyroid lobes , consistency , presence of nodules . 5. Tachycardia or atrial arrhythmia ,Systolic hypertension with wide pulse pressure ,Warm, moist, smooth skin 6. Lid lag ,Stare 7. Hand tremor, Muscle weakness 8. Dermatologic examination: - Pretibial myxedema - non- pitting edema, erythema and thickening of the skin, without pain or pruritus
Anatomical	**Thyroid uptake scan:** - Technetium-99m (99m Tc) - Iodine-123 (123 I)

Summary

Thyroid Disorders:

➔ Hyperthyroidism Or Hypothyroidism

➔ Others: Nontoxic goiter, Subacute Thyroiditis, Acute thyroiditis, Chronic thyroiditis, Thyroid Nodules, Thyroid Cancer.

<table>
<tr><th></th><th>Hyperthyroidism & Thyrotoxicosis</th><th>Hypothyroidism</th></tr>
<tr><td rowspan="4">Causes</td><td rowspan="4">- Diffuse toxic goiter (Graves' disease)
- Toxic adenoma (Plummer's disease)
- Toxic multinodular goiter
- Subacute thyroiditis
- Hyperthyroid phase of Hashimoto's thyroiditis
- Iodine-induced hyperthyroidism
- Thyrotoxicosis factitia
- ovarian struma</td><td>Primary:
- Hashimoto's thyroiditis.
- Radioactive iodine therapy
- thyroidectomy
- Excessive iodine intake (kelp, radiocontrast dyes)
- Subacute thyroiditis
- Iodide deficiency
- Other goitrogens such as lithium, amiodarone, antithyroid drug therapy</td></tr>
<tr><td>Secondary: Hypopituitarism due to
a- Pituitary adenoma b- pituitary ablative therapy c- pituitary destruction</td></tr>
<tr><td>Tertiary: Hypothalamic dysfunction</td></tr>
<tr><td>Peripheral resistance of thyroid hormone</td></tr>
<tr><td>Clinical Manifestation</td><td>Skin: Sweating, Moist warm skin, palmar erythema, thin hair.
Brain: Hyperthermia, Heat intolerance, Increase appetite, Anxiety, Hand tremor.
GIT: Loose bowel motion
Renal: Urinary frequency.
Heart: Palpitation, Sinus tachycardia, Atrial fibrillation.
Eye: eyelid lag, Eyelid retraction (staring gaze)
Bone: bone fracture, Osteoporosis, Hypercalcemia.
Muscles: muscle wasting & weakness, Hyperreflexia, Weight loss.
Reproductive: Female: Menstrual cycles disturbances (Oligo-or amenorrhea)/ Male: ED</td><td>General: Myxedematous Appearance Weight gain
Skin: Scaliness of skin, Brittle hair.
Brain: Cognitive dysfunction, Hypothermia, Cold Intolerance, Extreme Somnolence (sleepiness), Decrease Appetite
GIT: Constipation
Renal: Oliguria
Heart: Bradycardia Eye Periorbital Edema
Muscles: Proximal Myopathy, Fatigue, Delayed Relaxation Reflexes.
Reproductive:
Male>Loss of libido. Women>Menorrhagia.</td></tr>
</table>

	Specific manifestations in graves' disease: Orbitopathy (exophthalmos), Dermopathy (pretibial myxedema)..	
Diagnosis	**Biochemical:** - Clinical Hyperthyroidism: FT4 high, FT3 high, TSH low - Subclinical Hyperthyroidism: FT4 normal, FT3 normal, TSH low. - TSH Mediated Hyperthyroidism: FT4 high, FT3 high, TSH high. **Radiological:**Thyroid Scan **Serology:** Thyroid antibodies, TSH Receptor antibodies.	**Biochemical:** - Primary Hypothyroidism:High TSH, Low T4 - Secondary Hypothyroidism: Low TSH, Low T4 **Serology:** Thyroid antibodies **ECG**
Complications	**Thyrotoxic crisis (thyroid storm):** * Fever / Agitation * Altered mental status * Atrial fibrillation / Heart failure	1- **Myxedema coma** 2- **heart disease** 3- **neuropsychiatric disease**
Treatment	● **Anti-thyroid medications**: Propylthiouracil or methimazole. ● **Radioactive iodine therapy**: (131I) ● **Beta Blockers** ● **SSKI** ● **Thyroidectomy**	**Levothyroxine (T4) Replacement:** - Lower dose in elderly and higher dose in pregnancy and lactation

Questions

Q1) A 30-year-old woman complains of palpitations, fatigue, heat intolerance, and insomnia. She is otherwise healthy. She and her husband desire children and are not interested in contraception. On physical examination, her extremities are warm and she is tachycardic. There is diffuse thyroid enlargement and exophthalmos, as well as thickening of the skin in the pretibial area. Laboratory testing reveals a free T4 value of 3.2 ng/dL (normal 0.9-2.4) with an undetectably low TSH level. Radioiodine uptake at 24 hours is 42% (normal 10%-30%). What is the best treatment plan for this patient?

A. Propylthiouracil
B. Radioactive iodine
C. Propranolol
D. Thyroid surgery
E. Oral corticosteroids

Q2)On routine physical examination, a 28-year-old woman is found to have a thyroid nodule. She denies pain, hoarseness, hemoptysis, or local symptoms. Serum TSH is normal. Which of the following is the best next step in evaluation?

A. Thyroid ultrasonography
B. Thyroid scan
C. Surgical resection
D. Fine needle aspiration of thyroid

Q3) A 60-year-old woman comes to the emergency room in a coma. The patient's temperature is 32.2°C (90°F). She is bradycardic. Her thyroid gland is enlarged. There is diffuse hyporeflexia. BP is 100/60. Which of the following is the best next step in management?

A. Await results of T4 and TSH.
B. Obtain T4 and TSH; begin intravenous thyroid hormone and glucocorticoid.
C. Begin rapid rewarming
D. Obtain CT scan of the head.
e. Begin intravenous fluid resuscitation.

Q4) which of the following is contraindicated in patient suffering from exophthalmos?

A.RAI
B.propylthiouracil(PTU)

C.methimazole

Q5) which of the following tests is used to assess the severity of Graves disease ?

A.TSH
B.FREE T4
C.T3
D.UREA

Q6) A 25-year-old woman comes to the clinic for routine check up with no active symptoms. Serum TSH is elevated. free T3 and T4 are normal. What is the diagnosis?

A.Subclinical Hypothyroidism.
B.Euthyroid.
C.Mild Hypothyroidism.

Q7) For the case above, What's the next step in investigations?

A.Wait for symptoms to appear.
B.Start the patient on thyroxine.
C.Order thyroid Ab.

Q8) A 16-year-old girl presents to her GP complaining of a swelling in her neck which she has noticed in the last 2 weeks. She has felt more irritable although this is often transient. On examination, a diffuse swelling is palpated with no bruit on auscultation. The most likely diagnosis is:

A.Hyperthyroidism.
B.Simple goiter.
C.Thyroid carcinoma.

Q9) A 60-year-old woman presents to a physician complaining of swelling in her neck. Her past medical history is significant for rheumatoid arthritis and Sjogren syndrome. Physical examination reveals a mildly nodular, firm, rubbery goiter. Total serum thyroxine (T4) is 10 mg/dL, and third-generation thyroid-stimulating hormone (TSH) testing shows a level of 1.2 mIU/mL. Antithyroid peroxidase antibody titers are high, which of the following is the most likely diagnosis?

A.Hashimoto thyroiditis.
B.Euthyroid sick syndrome.
C.Subacute thyroiditis

Q10) A 20-year-old woman presents after recent upper respiratory infection. She complains of neck pain and heat intolerance. The thyroid is tender. Erythrocyte sedimentation rate is elevated; free thyroxine value is modestly elevated. What is the most likely diagnosis?

A. Struma ovarii.

B.Euthyroid sick syndrome.

C.Subacute thyroiditis.

ANS: 1-A,2-D,3-B,4-A,5-B,6-A,7-C,8-B,9-A,10-C