Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY

# Thyroid disorders

## Objectives :

1. Thyroid anatomy and physiology
2. Action of thyroid hormones
3. Thyroid function
4. Thyroid disorders:
   a. Goiter
   b. Hyperthyroidism
   c. Hypothyroidism

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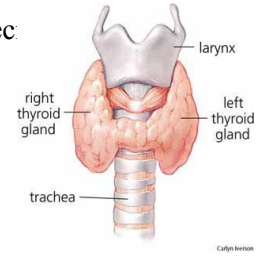
## Resources :

Doctor's slides + Team 436
Lecturer: Prof. Assim Alfadda & Dr. Aishah Ekhzaimy
Same as 436 slides: Yes
Step up

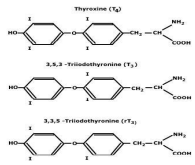
# Thyroid gland

- Thyroid gland is made up of follicles
- Has 2 lobes and connected by the isthmus
- Weigh 20 g, more volume in men, increase with age and bodyweight and dec intake
- Located in front of larynx




# Thyroid hormone

- Somatic development in adults
- Brain development in infants
- Fetal thyroid functions at 10-12 weeks of gestaion
- Maternal T4 reaches the fetus during development, if mother has hypothyroidism---------- preterm delivery, miscarriage, cognitive impairment of infant
- Main action of thyroid hormones by T3 : 80 % from peripheral conversion and 20 % produced by the thyroid itself.



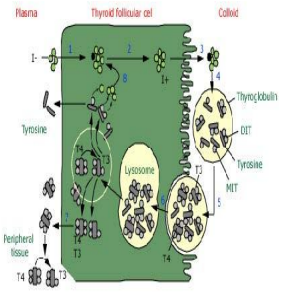
**Follicular cells of the thyroid is the main site of hormones synthesis**

- Mainly T4 and small amount of T3
- Iodine is needed to produce thyroid hormones
- Average adult requirement of iodine is 150 mcg a day, 220 mcg for pregnants, 290 mcg for lactating
- Source of iodine: dairy and seafood products

**Stored in the thyroglobulin in follicular cells of the thyroid gland**

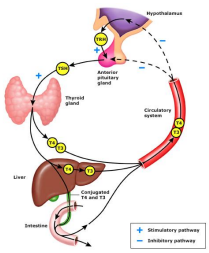
- 99.9 % of T4 and T3 are bound to protein in the blood: TBG, albumin, lipoprotein
- T4 and T3 synthesis and secretion is regulated by
- pituitary TSH.
- TSH is inhibited by T4 and T3, stimulated by TRH
- Extrathyroidal conversion of T4 to T3 is regulated by nutrition, illness, hormonal factors

## Thyroid hormones synthesis




# Thyroid hormone action

- Thyroid hormones act on the bone and bone development
- In children: delayed growth and epiphyseal growth
- In brain: cognitive impairment
- Act on cardiac muscle: tachy and bradycardia
- Regulate metabolic rate and little change in body weight




# Thyroid function

- TSH
- Free T4, FreeT3
- TRH
- TBG
- Thyroid antibodies: microsomal antibodies, TSH receptor antibodies, thyroglobulin antibodies

# Patients with thyroid disease:

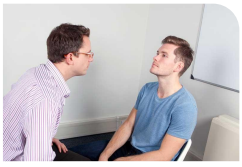
- Thyroid enlargement (goiter): diffuse or nodular
- Symptoms of hypothyroidism
- Symptoms of hyperthyroidism
- Complications of a specific form of hyperthyroidism-Graves' disease-which may present with:
  - Striking prominence of the eyes (exophthalmos)
  - Thickening of the skin over the lower leg (thyroid dermopathy)
- Liver enlargement = Hepatomegaly
- Spleen Enlargement = Splenomegaly
- Thyroid enlargement = Goiter

# History:

- Exposure to ionizing radiation (1- Affect thyroid function 2- Can cause cancer)
- Iodide ingestion:
  - Kelp
  - Iodide-containing cough preparation
  - IV Iodide-containing contrast media(1- Previous catheter 2- Previous CT scan with contrast)
- Lithium carbonate
- Residence in an area of low dietary iodide
- Family history
  - Thyroid disease
  - Immunologic disorders:(Autoimmune diseases often come together but do not cause each other)
    - Diabetes
    - Rheumatoid disease
    - Pernicious anemia
    - Alopecia
    - Vitiligo
    - Myasthenia gravis
    - MEN 2A

# Physical examination:

- Observe the neck, especially as the patient swallows



- Examine from the front, rotating the gland slightly with one thumb while palpating the other lobe with the other thumb

- Examine from behind, using three fingers and the same technique

- Determine the size of the thyroid lobes, consistency, presence of nodules

# Hypothyroidism Causes

Primary = Source of problem = thyroid itself
Secondary = Source of problem = pituitary
Tertiary = Source of problem = hypothalamus

| Primary | Secondary |
|---|---|
| 1. Hashimoto's thyroiditis: most common cause<br>○ With goiter<br>○ "Idiopathic" thyroid atrophy, presumably end-stage autoimmune thyroid disease, following either Hashimoto's thyroiditis or Graves' disease<br>○ Neonatal hypothyroidism due to placental transmission of TSH-R blocking antibodies<br>2. Iatrogenic—**second most common cause of primary hypothyroidism**; results from prior treatments of hyperthyroidism<br>a. Radioactive iodine therapy for Graves' disease<br>b. Subtotal thyroidectomy for Graves' disease or nodular goiter<br>c. Excessive iodine intake (kelp, radiocontrast dyes)<br>3. Subacute thyroiditis<br>4. Iodide deficiency<br>5. Other goitrogens such as lithium, amiodarone, antithyroid drug therapy<br>6. Inborn errors of thyroid hormone synthesis | Hypopituitarism due to:<br>A. Pituitary adenoma<br>B. Pituitary ablative therapy<br>C. Pituitary destruction |
| **Tertiary** | |
| Hypothalamic dysfunction (rare) | |
| **Peripheral resistance of the action of thyroid hormone**<br>The thyroid axis is normal but the issue is on tissues' receptors | |

# Pathogenesis

- Thyroid hormone deficiency affects every tissue in the body, so that the symptoms are multiple
- 1-Accumulation of glycosaminoglycans-mostly hyaluronic acid- in interstitial tissues
- 2-Increase capillary permeability to albumin
- Interstitial edema (skin, heart muscle, striated muscle)

# Clinical presentations and findings:

**Adults:** The most striking symptom of hypothyroidism is myxedema ( Hand, lower limbs, face, periorbital, carpal tunnel, heart and etc..)

- Common feature: easy fatigability, coldness, **slight** weight gain **(10 to 30 lb)—patients are not typically obese**, constipation, menstrual irregularities (Delay pregnancy,Delay fertility,Occurs for both hypo and hyperthyroidism), and muscle cramps.
- Physical findings: cool rough dry skin, puffy face and hands, hoarse husky voice, and slow reflexes, yellowish skin discoloration.

## Cardiovascular

- Bradycardia
- Decreased cardiac output
- Low voltage ECG (because of pericardial effusion , so the signals won't reach the electrodes )
- Cardiomegaly
- Pericardial effusion

## Pulmonary Function

- Shallow and slow respiration
- Respiratory failure

## Gastrointestinal

- Chronic constipation
- Ileus

## Anemia

- Impaired hemoglobin synthesis
- Iron deficiency
- Folate deficiency
- Pernicious anemia, with B12 deficiency megaloblastic anemia
- Some are related to the other associated autoimmune and chronic diseases, and some are related to GUT Edema which it would decrease absorption of necessarily components of the blood such as folate and iron

## Neuromuscular system

- Severe muscle cramps
- Paresthesias
- Muscle weakness
- **Carpal tunnel syndrome**

## Central Nervous System

- Chronic fatigue
- Lethargy
- Decreased concentration
- Anovulatory cycles and infertility
- Menorrhagia
- Depression
- Agitation

## Renal function

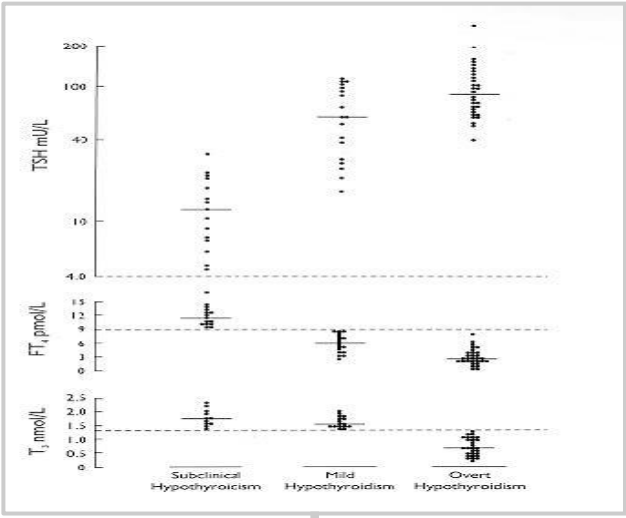
- Impaired GFR
- Water intoxication

## Diagnosis:

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 .

- Low serum FT4. Not in the first stage because the body would maintain it.
- Elevated serum TSH. First thing to be affected
- Thyroid antibodies.To look for causes 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 .
- TRH stimulation test. Expensive, we do not do it in the clinical practice.
- Increased antimicrosomal antibodies (Hashimoto thyroiditis).
- Other laboratory value abnormalities that may be present:

a. Elevated LDL and decreased HDL levels.
b. Anemia—mild normocytic anemia is the most common.




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.

Subclinical has a debate on whether you treat or not.
Treat if the patient:
• Symptomatic
• Pregnant
• Adolescent 9-15 since they're are growing
• Dyslipidemic( LDL receptors) People

## Complications:

1. Myxedema coma
   - The end stage of untreated hypothyroidism
   - Progressive weakness, stupor, hypothermia, hypoventilation, hypoglycemia, hyponatremia, water intoxication, shock, and death.
   - Associate illnesses 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.

Fluid accumulation can occur with hypothyroidism, you need to be cautious with fluid prescription and administration.

2. Myxedema and heart disease
3. Hypothyroidism and neuropsychiatric disease

(patient with heart disease on levothyroxine treatment can get or aggravate heart problems , because he has low metabolism then sudden increase in the metabolism happens so the heart can get ischemic because you're increasing heart's demand or worsen the condition)

# Treatment:

Thyroxine is the safest drug that you will come upon in medical practice but needs to be used and dosed appropriately.
We need 6 weeks to follow up thyroid function test because the t1/2 of thyroxine is 7 days to know whether it is normal or abnormal.
If it is abnormal, think about medication compliance, dosage or interactions with other drugs

## Hypothyroidism

- Levothyroxine (T4).
- Follow serum Free T4 and TSH
- 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)
- 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

## Myxedema coma

- 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
- Active rewarming of the body in contraindicated

# 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. Active rewarming of the body is 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. Besides, by default hypothyroid patients have low cardiac output. |
| 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) |

# Treatment:

### Myxedema with heart disease

- Start treatment slowly in long standing hypothyroidism and in elderly patients particularly those with known cardiovascular disease
- 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

- 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: hyperthyroidism symptoms may occur:
- Cardiac symptoms
- Osteopenia and osteoporosis

# Hyperthyroidism & Thyrotoxicosis

To clarify the two concepts:
Thyrotoxicosis factitia (exogenous thyrotoxicosis caused by the ingestion of exogenous thyroid) is not hyperthyroidism. Instead, is thyrotoxicosis.

**Definitions:**

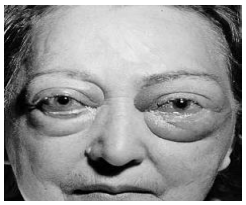
- Thyrotoxicosis: is the clinical syndrome that results when tissues are exposed to high levels of circulating thyroid hormone
- Hyperthyroidism: is the hyperactivity of the thyroid gland

**Conditions associated with thyrotoxicosis:**

- Diffuse toxic goiter (Graves' disease). Most common
- Toxic adenoma (**Plummer's disease**)
- Toxic multinodular goiter. These nodules are autonomous means independent from TSH control.
- Subacute thyroiditis. it's an inflammatory process that is caused by viruses or chemicals that will disturb the integrity of hormones storage causing them to be released in the circulation. " Not an autoimmune problem" It can cause transient hyperthyroidism due to leakage of hormone from inflamed thyroid gland. This is followed by a euthyroid state and then a hypothyroid state
- Hyperthyroid phase of Hashimoto's thyroiditis
- Thyrotoxicosis factitia. Factitia means artificial
- Rare: ovarian struma, metastatic thyroid carcinoma (follicular), hydatidiform mole, TSH secreting pituitary tumor, pituitary resistance to T3 and T4

# Diffuse Toxic Goiter (Graves' disease):

- ★ Most common form of thyrotoxicosis
- ★ Females > Males
- ★ Features:
  - Thyrotoxicosis
  - Goiter
  - Orbitopathy (exophthalmos)
  - Dermopathy (pretibial myxedema)

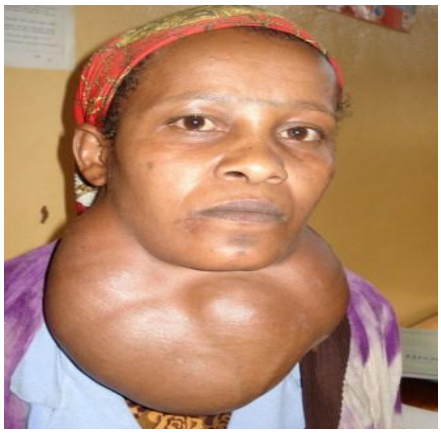


-Exophthalmos assessment is done by the sides and with exophthalmometer.
-Chemosis is the swelling (or edema) of the conjunctiva. This fluid can be spoiled out when you press swelling.


Elderly patient that might have Apathetic hyperthyroidism because of the thick skin in lower limb (pretibial myxedema)

# Goiter

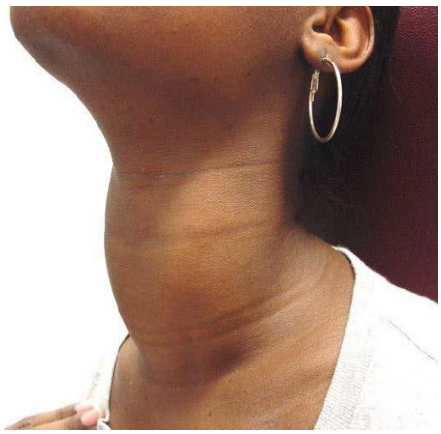
- Goiter: chronic enlargement of thyroid gland not due to neoplasm.
- Endemic Goiter: common in china and central africa
- Sporadic Goiter: multinodular goiter
- Familial



- Hashimoto's thyroiditis: in early stage
- Graves' disease: due to chronic stimulation of TSH receptor
- Diet: cabbage, Caulifower
- Chronic iodine excess
- Medication: lithium in 6%
- Neoplasm

- Assess thyroid function by :
  - Free T4, FT3
  - TSH
  - Ultrasound neck

# Goiter-non Toxic



- Thyroxine suppression therapy: not useful
- Surgery:
  - If pressure symptoms
  - Malignancy
  - Lymphadenopathy
- Radioactive iodine therapy

# Diffuse Toxic Goiter (Graves' disease):

**Symptoms**
a. Nervousness, insomnia, irritability
b. Hand tremor, hyperactivity, tremulousness
c. Excessive sweating, heat intolerance
d. Weight loss despite increased appetite
e. Diarrhea
f. Palpitations (due to tachyarrhythmias)
g. Muscle weakness

★ Etiology
- Autoimmune disease of unknown cause
- There is a strong familial predisposition
- Peak incidence in the 20- to 40- year age group

★ Pathogenesis "all are theories"
- 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

In Graves' disease autoantibodies bind the receptor for TSH and mimic the normal action of TSH, activating adenylate cyclase and resulting in production of the thyroid hormones.
Unlike TSH, the autoantibodies are not regulated, and consequently they overstimulate the thyroid.

★ Diagnosis
- Elevated FT4
- Suppressed TSH
- Eye signs

\+ → No further test
\- → Thyroid scan

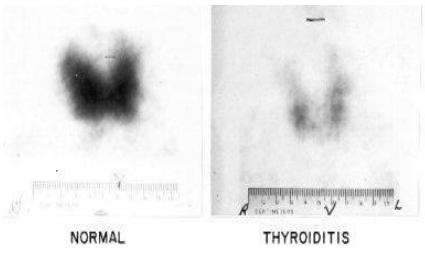
You have to rule out subacute thyroiditis by radioiodine uptake that would be low. In comparison to graves which will be high.

# Radioiodine uptake scan:

Low uptake = Cold nodule
High uptake = Hot nodule

This is cold nodule which carries 10-15% risk of cancer in comparison to hot nodule which carries 3% risk of cancer. Heterogenous. Some are hot and other are cold.

- Elevated uptake:
  - Graves' disease
  - TMN
- Low uptake:
  - Spontaneous resolving hyperthyroidism
  - Subacute thyroiditis
  - Thyrotoxic phase of Hashimoto's thyroiditis
  - Iodine loaded patients
  - Patients on LT4 therapy
  - Struma ovarii



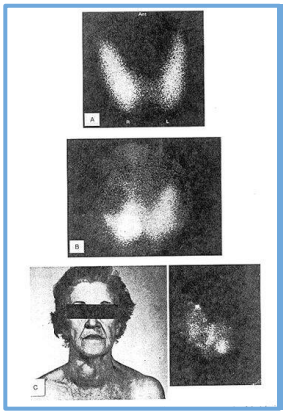



Figure 6-6. Thyroid Scans. a.Normal thyroid imaged with 123I. b.Cold nodule in the right lobe imaged by 99mTc. c.Elderly woman with obvious multinodular goiter and the corresponding radioiodide scan on the right.

## Diagnosis:

- TSH-R Ab [stim]
- Free T3
- Atypical presentations:
  - Thyrotoxic periodic paralysis. Paralysis in case of excessive thyroid hormones related to K disturbance.
  - Thyrocardiac disease. A-Fib, IHD or palpitations
  - Apathetic hyperthyroidism. No symptoms at all
  - Familial dysalbuminemic hyperthyroxinemia

## Complications:

**Hyperthyroidism in the Elderly**

- In the elderly, classic symptoms of hyperthyroidism (e.g., nervousness, insomnia, hyperactivity) may be absent. The only manifestations may be weight loss, weakness, and/or atrial fibrillation.
- Consider hyperthyroidism before assuming that an elderly patient with unexplained weight loss has depression or occult malignancy.

- Thyrotoxic crisis (thyroid storm) **This is a rare, life-threatening complication**
  - Predisposing conditions*
  - Clinical features:
    - Fever / Agitation / restlessness (cannot sit on a chair)
    - Altered mental status
    - Atrial fibrillation / Heart failure

- characterized by an acute exacerbation of the manifestations of hyperthyroidism. *There is usually a precipitating factor, such as infection, DKA, or stress (e.g., severe trauma, surgery, illness, childbirth). High mortality rate: up to 20% of patients enter a coma or die. Clinical manifestations include marked fever, tachycardia, agitation or psychosis, confusion, and GI symptoms (e.g., nausea, vomiting, diarrhea).
- Provide supportive therapy with IV fluids, cooling blankets, and glucose. Give antithyroid agents (PTU every 2 hours). Follow with iodine to inhibit thyroid hormone release. Administer β-blockers for control of heart rate. Give dexamethasone to impair peripheral generation of T3 from T4 and to provide adrenal support.

## Treatment of Graves' disease:

Always remember:
1-Medication
2-Radioactive therapy
3-Surgery

- Antithyroid drug therapy Blocks thyroid hormone synthesis
  - Propylthiouracil or methimazole
  - Spontaneous remission 20-40%
  - Relapse 50-60%
  - Duration of treatment 6 months – years
  - Reactions to antithyroid drugs

Possible side effects:
1-Agranulocytosis
Symptoms of agranulocytosis may include:
-Sores in the mouth, throat, or gastrointestinal tract.
-Chronic infections of the gums, throat, or skin.
-Fever.
2- Jaundice

Management: Stop anti-thyroid medications
Propylthiouracil "is safe for pregnant ladies

- Surgical treatment
  - Subtotal thyroidectomy
  - Preparation for surgery
  - Complications:
    - Hypothyroidism/ hypoparathyroidism
    - Recurrent laryngeal nerve injury

You do surgery if the meds and radioactive iodine fail or one of the following:
1-Very large goiter with compressible features
2-Grave's disease with malignancy

Symptoms of recurrent laryngeal nerve injury:
1-Unilateral vocal fold paralysis (post-operative hoarseness or breathiness. also, dysphagia and aspiration)
2-Bilateral vocal fold paralysis (airway obstruction), usually thi occurs with total thyroidectomy

- Radioactive iodine therapy
  - $^{131}I$ is most commonly used
  - **Dose:**

    $^{131}I_{(uci/g)}$ x thyroid weight x 100/ 24-hr RAI uptake
- b-blockers to treat symptoms
- SSKI Supersaturated potassium Iodine after giving anti-thyroid medications

You will change the patient of being hyperthyroid to be hypothyroid. In practice, you would be asked what is the benefit?
The answer is thyroxine is much more safer than antithyroid drugs. Besides, it can be controlled and adjusted easily.

## Treatment of Graves' Disease Complications:

- Thyrotoxic crisis
- Orbitopathy refer to ophthalmologist (reconstruction surgery can be done)
- Thyrotoxicosis and pregnancy Very dangerous situation. Why?
  - 1- we cannot give radioactive iodine
  - 2-Surgery is not the best choice except 2nd trimester.
  - 3-Anti-thyroid can cause hypothyroidism which is disastrous condition in pregnancy.

## Treatment of Other Forms of Thyrotoxicosis:

if the thyroid has an adenoma producing thyroxine :
1)Meds 2)radio-Iodine(if it's small) 3)surgery (preferably if it's big
Titrate thyroid hormones to normal before you proceed to radioactive iodine or surgery.

- Toxic adenoma
- TMN
- Amiodarone
- Subacute thyroiditis We don't give them anti-thyroid since the issue is destruction of the hormones storage.We can give B-blockers, aspirin or in rare causes steroids
- Thyrotoxicosis factitia Stop the medication. Requires a very good history.
- Struma ovarii

## Other Thyroid Disorders:

- Nontoxic goiter
- Subacute thyroiditis (De Quervain's)
- Chronic thyroiditis
- Acute thyroiditis
- Thyroid nodules
- Thyroid cancer

Detecting or measuring thyroglobulin (TG) in previously treated patients with thyroid cancer is very crucial because it can detect any cancer recurrence but it has to be done understimulation. High = positive , Low = negative

- Signs
  **a. Thyroid gland:**
  - Graves disease: a diffusely enlarged (symmetric), nontender thyroid gland; a bruit may be present.
  - Subacute thyroiditis: an exquisitely tender, diffusely enlarged gland **(with a viral illness).**
  - Plummer disease and Hashimoto thyroiditis (if multinodularity is present): thyroid gland is bumpy, irregular, and asymmetric.
  - Toxic adenoma: single nodule with an otherwise atrophic gland.

  **b. Extrathyroidal**
  - Eyes: Proptosis, due to edema of the extraocular muscles and retro-orbitaltissue, is a hallmark of Graves disease (but not always present). Irritation and excessive tearing are common due to corneal exposure. Lid retraction may be the only sign in milder disease . Lid lag may be present.
  - Cardiovascular effects: arrhythmias (sinus tachycardia, atrial fibrillation, and premature ventricular contractions), elevated BP
  - Skin changes: warm and moist, pretibial myxedema (edema over tibial surface due to dermal accumulation of mucopolysaccharides)
  - Neurologic: brisk deep tendon reflexes, tremor

## Summary

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

## Summary

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

# Questions

1-A 42-year-old woman presents with visual disturbances. She reports having double vision which was intermittent initially but has now become much more frequent. In addition, she becomes breathless very easily and experiences palpitations. On examination, raised, painless lesions are observed on the front of her shins and finger clubbing. The most likely diagnosis is:
A. De Quervain's thyroiditis
B. Thyroid storm
C. Graves' disease
D. Plummer's disease

2-21 A 47-year-old woman is referred to the endocrine clinic complaining of a two- month history of tiredness. Despite wearing several items of clothing, the patient appears intolerant to the room temperature. She has noticed an increase in weight, particularly around her waist. The most appropriate investigation is:
A. Radioiodine scan
B. Thyroid stimulating hormone (TSH)
C. Total tetraiodothyronine level (T4)
D. Tri-iodothyronine level (T3)

3-A 27-year-old woman presents with palpitations, fatigue, heat intolerance, and insomnia. She has an otherwise unremarkable medical history. She is on no medications and does not use illicit drugs, weight loss products, or caffeine. On physical examination, her extremities are warm and she is tachycardic. Her neck shows diffuse, nontender thyroid enlargement. She has mild proptosis, as well as thickening of the skin in the pretibial area. Her laboratory values show a free T4 value of 3.2 ng/dL (normal 0.9-2.4), and increased radioiodine uptake at 24 hours. Which of the following statements about the pathogenesis of her disease process is most accurate?
A.Antibodies against TSH cause its level to appear low when in reality it is being overproduced, leading to high levels of T4.
B. Immune globulins produced in the thyroid, lymph nodes, and bone marrow stimulate the thyroid directly to produce high levels of T4.
C. Microscopic thyroid lesions present in the enlarged thyroid gland produce T4 in an autonomous and unregulated fashion.
D. Multiple nodules that will be evident on a thyroid ultrasound secrete a TSH analog which leads to hyperthyroidism.

4-A 45-year-old G2P2 woman presents for annual examination. She reports regular menstrual cycles lasting 3 to 5 days. She exercises five times per week and reports no difficulty sleeping. Her weight is stable at 140 lb and she is 5 ft 8 in tall. Physical examination is unremarkable. Laboratory studies are normal with the exception of a TSH value of 6.6 mU/L (normal 0.4-4.0 mU/L). Free T4 is normal. Which of the following represents the best option for management of this patient's elevated TSH?
A. Repeat TSH in 3 to 6 months and reassess for symptoms of hypothyroidism.
B. Begin low-dose levothyroxine (25-50 μg/d).
C. Recommend dietary iodide supplementation.
D. Order thyroid uptake scan.

# Questions

5- 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.

6-A 38-year-old female presents to your office with chief complaint of fatigue and weight gain for the past 5 to 6 months. Her fatigue has also affected her performance at work, where she has difficulty concentrating on tasks. She recently began losing hair. She feels more tired than usual after work and has difficulty playing with her children in the evening. She did not have any of these symptoms until 6 months ago. She denies hot/cold intolerance. Weight has been relatively stable but she has gained ~10 lb in the past 6 months despite attempting to eat healthy and exercise a few times weekly. She is generally happy and denies any recent mood changes.
PMH is insignificant. The patient smokes five to six cigarettes a day and drinks alcohol socially. She takes birth control pills. HR 55, BP 120/80 mmHg, RR 16, BMI 31. Physical examination reveals a pleasant female, oriented and appropriate. ENT examination reveals normal pharynx, no neck fullness, and no palpable thyroid nodules. Abdomen is soft, nontender. Skin examination reveals no lesions/rashes and there is no lower extremity edema. She donated blood last week and was told that her Hgb was normal. What is the appropriate next step in managing this patient?
A. US thyroid
B. Thyroid uptake scan
C. FNA
D. TSH

7-A 53-year-old female presents to the hospital with abdominal pain. She is diagnosed with cholecystitis and has a cholecystectomy performed. The following day she complains of palpitations. On questioning she has had an irregular heart beat off/on for the past few months but acutely worsened during this episode. She also notes a 15-lb weight loss over the past month. She denies dizziness, syncope, dyspnea, or chest pain. She has a known history of hyperlipidemia but has otherwise been healthy. Medications include ASA and atorvastatin. Vitals: Temperature = 102.4°F, BP = 155/88 mm Hg, pulse = 134. Oxygen saturation at room air = 96%. Physical examination: patient is agitated and appears confused, sometimes answering questions inappropriately. Skin is diaphoretic. Neck is supple without tenderness and no palpable nodules or enlargement. Cardiac examination reveals an irregular rhythm, tachycardia, and no murmurs. ECG confirms atrial fibrillation with rapid ventricular response. TSH is <0.01 mU/L.
What is the most appropriate next step in the management of this patient?
A. Radioactive iodine uptake scan
B. Iodine
C. US thyroid
D. Propranolol

# Questions

8- A 33-year-old female presents to your office with the complaint of insomnia and difficulty concentrating at work for several weeks. She reports a 20-lb weight loss over the past 2 to 3 months, despite eating more. When questioned, she reports that she frequently feels “hot and sweaty” at work and at home. She denies chest pain or palpitations but does have diarrhea frequently. Vital signs are: Temperature = 98.9°F, RR = 15, BP = 130/80, pulse = 98. She appears worried. On physical examination, she has warm and moist skin. She has a slight hand tremor. On palpation of her thyroid, you note a diffusely enlarged thyroid gland that is nontender. Which of the following is the best next step in management?

A. Free T4 levels
B. Thyroid-stimulating hormone (TSH) levels
C. Thyroglobulin levels
D. Radioactive iodine uptake (RAIU) scan
E. A fine-needle aspiration (FNA) biopsy

9-A 36-year-old woman presents with delirium and congestive heart failure. Her husband indicates that she has been losing weight and becoming more anxious and irritable over the past 3 months. Over the past several weeks she has developed dyspnea and peripheral edema. She has previously been healthy and takes no medications. Her husband says that she drinks alcohol moderately and has never used illicit drugs. On physical examination, she is awake, anxious, and confused. Her temperature is 38°C (100°F) and her heart rate is 142 and regular. She has jugular venous distension to 16 cm above the sternal angle as well as bibasilar rales. In addition, she has a diffuse goiter with a soft bruit over each lobe, as well as a stare expression and exophthalmos. Chest x-ray (CXR) shows pulmonary edema and cardiomegaly. Her ECG reveals sinus tachycardia but is otherwise unremarkable. What is the best approach to management of this patient?

A. Admit to the general medicine ward, obtain serum-free T4 and TSH, order a radioiodine uptake and scan, and begin furosemide 40 mg IV daily.
B. Order free T4 and TSH, start the patient on propranolol 20 mg po tid and Lasix 40 mg po bid, obtain a radioiodine uptake and scan, and follow closely as an outpatient.
C. Obtain free T4, TSH, and thyroid-stimulating immunoglobulin levels, begin methimazole 10 mg po tid, and follow closely as an outpatient.
D. Admit to the general medicine ward, obtain blood and urine cultures and an echocardiogram, andbegin treatment with broad-spectrum antibiotics and furosemide.
E. Admit the patient to the intensive care unit (ICU), order free T4 and TSH, and begin high-dose propranolol, propylthiouracil, potassium iodide, corticosteroids, furosemide, and acetaminophen.

# Answers

1- (C)

2- (B)

3- (B)

4- (A)

5- (B)

6- (D)

7- (D)

8- (B)

9- (E)

(1) C Graves' disease (C) is the most common cause of hyperthyroidism. The condition is due to IgG antibodies binding to the TSH receptor, this in turn causes excess production of thyroid hormone. The antibodies also bind to other areas of the body such as the extraocular muscles leading to gaze abnormalities, the shins causing raised lesions known as 'pretibial myxoedema' and rarely the fingers causing clubbing known as 'thyroid acropachy'. These collective signs are only seen in Graves' disease, hence it is the only correct answer. De Quervain's thyroiditis (A) is a transient thyroid state most likely due to a viral infection. The patient usually complains of a fever and painful neck with some signs of hyperthyroidism, such as tachycardia, as well as raised ESR levels. A few weeks later, the patient suffers from transient hypothyroid symptoms before returning to a euthyroid state. Plummer's disease (D) is a solitary nodule in the thyroid gland producing excess thyroid hormones. It is usually refractory to antithyroid treatment. A thyroid storm or crisis (B) is a rapid deterioration in patients suffering from hyperthyroidism, often stimulated by a stressor such as infection. Patients present with acute-onset, severe tachycardia, distress and hyperpyrexia.

(4)-A. In this patient with a TSH below 10 μU/L and no symptoms of hypothyroidism, the diagnosis is subclinical hypothyroidism. Recommendations include checking a free thyroxine level (it should be normal in subclinical hypothyroidism) and repeating the TSH in 3 to 6 months to monitor for progression toward overt hypothyroidism. The patient should be informed about the symptoms of hypothyroidism. Thyroxine therapy is not currently recommended for most asymptomatic patients with a TSH level below 10 mU/L. One exception is women contemplating pregnancy, whose TSH should be lowered with l-thyroxine to less than 2.5 mU/L before conception. Although an abnormal TPO Ab increases the risk of progression to overt hypothyroidism, it does not affect your present management. Thyroid uptake scan may be useful in the diagnosis of hyperthyroidism, but not in possible hypothyroidism. Iodide deficiency is not seen in the United States because of dietary iodide supplementation although it could be considered in immigrants or refugees from developing countries.

(5)The clinical picture strongly suggests myxedema coma. Unprovoked hypothermia is a particularly important sign. Myxedema coma constitutes a medical emergency; treatment should be started immediately. Should laboratory results fail to support the diagnosis, treatment can be stopped. An intravenous bolus of levothyroxine is given (200-500 μg loading dose), followed by daily intravenous doses (50-100 μg). If high doses are used, the patient should be carefully monitored for cardiac arrhythmias. Impaired adrenal reserve may accompany myxedema coma, so parenteral hydrocortisone is given concomitantly. Intravenous fluids are also needed but are less important than thyroxine and glucocorticoids; rewarming should be accomplished slowly, so as not to precipitate cardiac arrhythmias. If alveolar ventilation is compromised, then intubation may also be necessary. Hyponatremia and an elevated Pco2 are laboratory markers of severe myxedema. CT of the head would not be the first choice, since a structural brain lesion would not explain the hypothermia, diffuse goiter, or hyporeflexia seen in this case.

(9)This patient has thyroid storm, a medical emergency. The presence of fever, severe tachycardia, congestive heart failure, and CNS changes (delirium, psychosis, seizure, orcoma) help separate thyroid storm from uncomplicated hyperthyroidism. Other factors that point toward storm or impending storm include atrial fibrillation, abdominal symptoms, jaundice, and the absence of a precipitating event. Even with treatment, the mortality of thyroid storm can be 10% to 20%, so admission to an intensive care unit for close monitoring is mandatory. Propranolol, generally contraindicated in decompensated congestive heart failure, improves the high-output CHF and, in high doses, helps block conversion of T4 to the active hormone T3. Propylthiouracil blocks the uptake and organification of iodide by the thyroid gland, and oral iodides prevent the release of preformed T4 and T3 from the thyroid gland. Relative adrenal insufficiency is often present, so corticosteroids are administered routinely in thyroid storm. Patients with mild to moderate hyperthyroidism are usually evaluated and treated as an outpatient. Impending or threatened thyroid storm can be managed on the general medicine ward or in the ICU as clinically indicated, but overt thyroid storm (as in this patient) requires ICU care. If an outpatient has a diffuse goiter and if the cause of hyperthyroidism is unclear, radioiodine uptake can be measured to distinguish Graves disease (normal or increased RAI uptake) from painless thyroiditis (low RAI uptake). In thyroid storm, however, immediate treatment takes precedence over measuring the 24-hour radioiodine uptake. Furthermore, thyroiditis rarely, if ever, causes thyroid storm. Thyroid-stimulating immunoglobulin assays are rarely needed to diagnose Graves disease. Methimazole is often used in mild to moderate hyperthyroidism because of ease of dosing, but propylthiouracil blocks T4 to T3 conversion and should be used in thyroid storm. Although the febrile, tachycardic patient with hyperthyroidism can appear septic, other features of this case strongly suggest that thyroid storm, not infection, is the cause of her illness. Antibiotics without proper management of her hyperthyroidism would probably prove fatal.