Thyroid Gland

- ***Anatomy:***

The thyroid gland is located in the front of the neck attached to the lower part of the larynx and to the upper part of the trachea, so it moves with swallowing. It has two lobes. These lobes are connected by isthmus. Each lobe is about 4 cm long and 1 to 2 cm wide.

- ***Histology:***

The thyroid is composed of spherical follicles that selectively absorb iodine from the blood for production of thyroid hormones, and also for storage of iodine in thyroglobulin. Twenty-five percent of the body's iodide ions are in the thyroid gland.

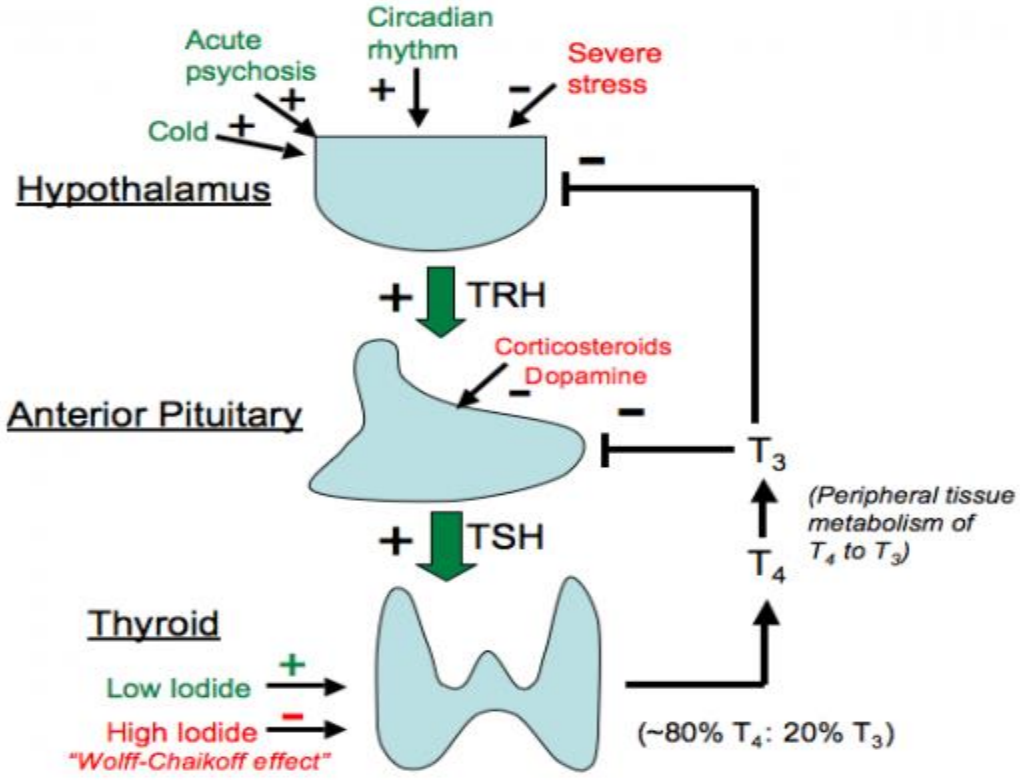


Figure 1: show secretion of thyroid hormones

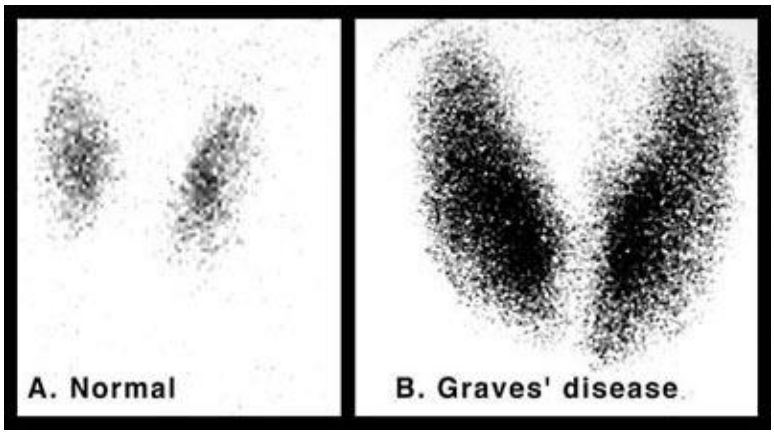
- ***Actions of thyroxin hormone:***

1. Increases cardiac output and increases heart rate
2. Increases ventilation rate and oxygen consumption
3. Increases basal metabolic rate
4. potentiates the effects of catecholamine (i.e. increases sympathetic activity)
5. Potentiates brain development
6. Thickens endometrium in females

7. Increases metabolism of proteins (i.e. they have a catabolic action).
8. Increases absorption and utilization of glucose
9. It lowers cholesterol.

- ***Thyroid function tests:***

1- ***TSH*:** (TSH, thyrotropin) is elevated in hypothyroidism and secondary hyperthyroidism and decreased in hyperthyroidism and secondary hypothyroidism. It is the most sensitive test for thyroid hormone function.
2- ***Total T4:*** rarely measured now, having been largely superseded by free thyroxin tests, generally elevated in hyperthyroidism and decreased in hypothyroidism. It is usually slightly elevated in pregnancy secondary to increased levels of thyroid binding globulin (TBG).
3- ***Free T4*:** generally elevated in hyperthyroidism and decreased in hypothyroidism. Reference ranges depend on the method of analysis.
4- ***Estimation of T3***: to diagnose T3 toxicosis.
5- ***T3 resin uptake***: measures the free TBG, unoccupied sites og TBG. Radioactive T3 added to patient serum, fixed to binding sites of TBG, the remaining unabsorbed radioactive T3 is absorbed into a resin & its radioactivity is measured. It decreased in hypothyroidism and increased in hyperthyroidism.
6- ***Free thyroxine index:*** obtained by multiplying the total T4 with T3 resin uptake. FTI is considered to be a more reliable indicator of thyroid status in the presence of abnormalities in plasma protein binding.
7- ***TSH stimulation test***: differentiate 1ry from 2ry hypothyroidism, we give TSH to the patient;
-increase of thyroxin in 2ry hypothyroidism, but it will not be increased in 1ry hypothyroidism.
8- ***Calcitonin*:** Increased in medullary carcinoma.
9- ***Thyroid sonar*:** differentiate cystic from solid nodules and detect retrosternal extension.
10- ***Thyroid scan*:** using radioactive iodine or Technetium uptake. High uptake in hyperthyroidism or Iodine deficiency. Low uptake present in hypothyroidism or thyroiditis. Differentiate functioning (hot) nodules from non-functioning (cold) nodules.



11- ***Fine needle biopsy***: for pathological assessment.

12- ***Immunologic tests*:**

-Antithyroglobulin antimicrosomal antibodies in hashimoto thyroiditis.

-Thyroid stimulating immunoglobulin (TSI) marker of Graves' disease.

GOITER

Definition

- A goiter is an enlarged thyroid gland, and it may be diffuse or nodular. A goiter may extend into the retrosternal space, with or without substantial anterior enlargement.
- Because of the anatomic relationship of the thyroid gland to the trachea, larynx, superior and inferior laryngeal nerves, and esophagus, abnormal growth may cause a variety of compressive syndromes.
- Thyroid function may be normal (nontoxic goiter), overactive (toxic goiter), or underactive (hypothyroid goiter).

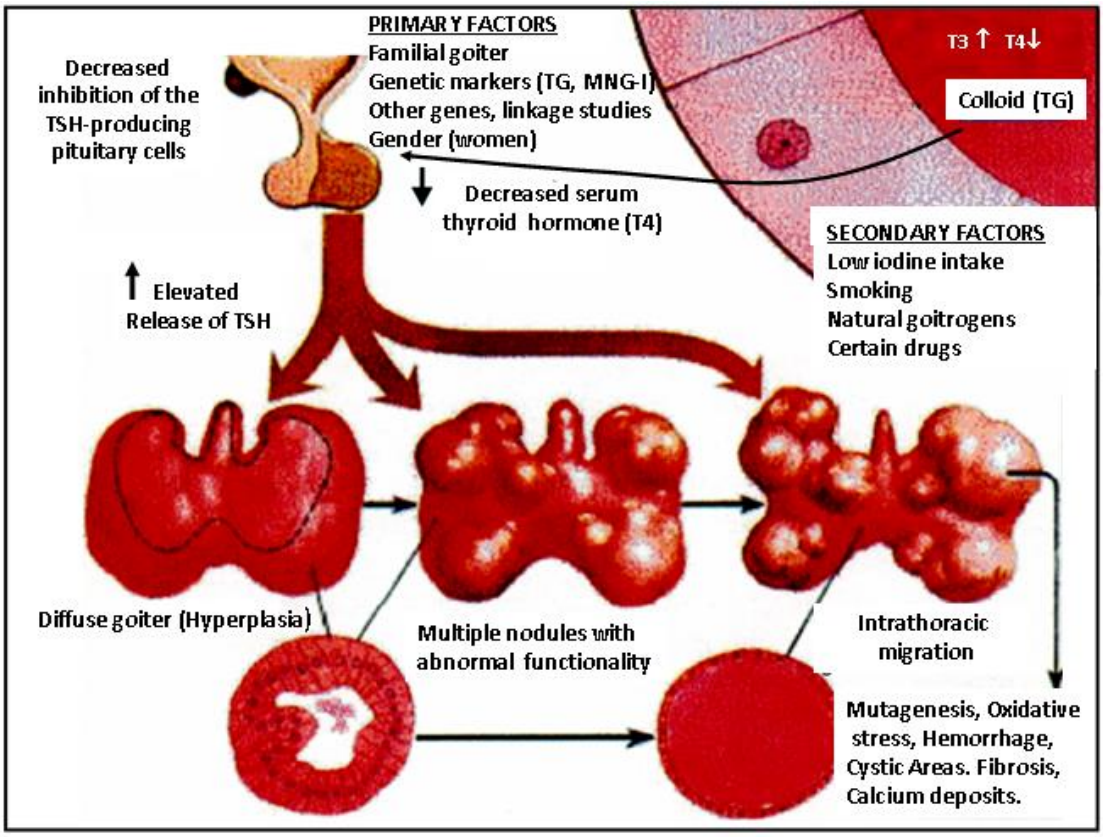


Figure 2: show development of goiter & subtypes

Pathogenesis:

- When diffuse enlargement of the thyroid occurs in the absence of nodules and hyperthyroidism, it is referred to as a ***diffuse nontoxic goiter***. This is sometimes called ***simple goiter***, due to the absence of nodules, or ***colloid goiter***, due to the presence of uniform follicles that are filled with colloid.
- Worldwide, diffuse goiter is most commonly caused by iodine deficiency and is termed ***endemic goiter*** when it affects >5% of the population.

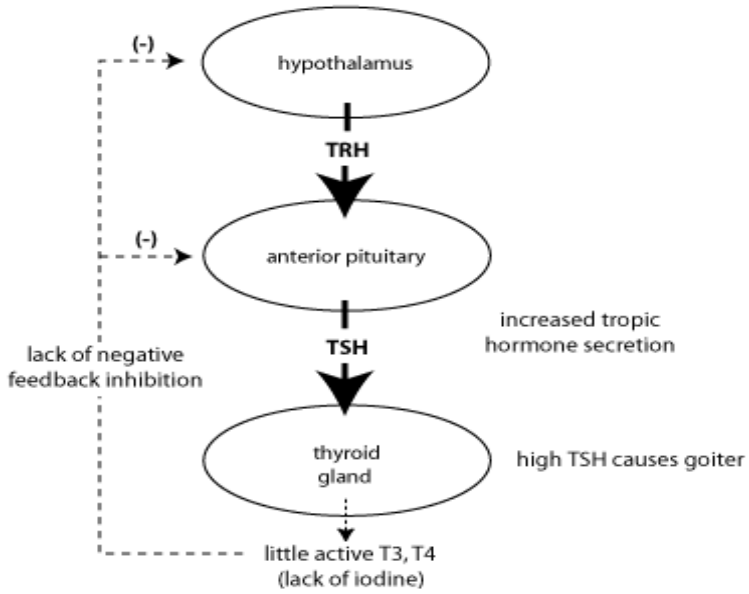


Figure 3: show pathogenesis of goiter

- In non-endemic regions, ***sporadic goiter*** occurs, and the cause is usually unknown.
- Thyroid enlargement in teenagers is sometimes referred to as ***juvenile goiter***. In general, goiter is more common in women than men, probably because of the greater prevalence of underlying autoimmune disease and the increased iodine demands associated with pregnancy.
- In ***iodine-deficient areas***, thyroid enlargement reflects a compensatory effort to trap iodide and produce sufficient hormone under conditions in which hormone synthesis is relatively inefficient. Somewhat surprisingly, TSH levels are usually normal or only slightly increased, suggesting increased sensitivity to TSH or activation of other pathways that lead to thyroid growth.
- Iodide appears to have direct actions on thyroid vasculature and may indirectly affect growth through vasoactive substances such as endothelins and nitric oxide.
- Endemic goiter is also caused by exposure to environmental ***goitrogens*** such as cassava root, which contains a thiocyanate; vegetables of the Cruciferae family (known as cruciferous vegetables) (e.g., Brussels sprout, cabbage, and cauliflower)
- Though relatively rare, inherited defects in thyroid hormone synthesis including abnormalities at each step in hormone synthesis, lead to a diffuse nontoxic goiter.

- TSH-dependent hyperplasia→→autonomy may be due to mutations that occur with cell division in the oncogen that activate the **G protein** in the cell membrane (called **GSP** oncogen).
- When a small group of thyroid cells, inflammatory cells, or malignant cells metastatic to the thyroid is involved, a thyroid nodule may develop.
- If nodule can concentrate iodine→ **hot nodule** or cannot→ **cold nodule**
- If Can synthesize thyroglobulin→ **colloid nodule**…. If cannot→ **microfollicular nodules**. Hemorrhage and necrosis→ **cyst** formation.
- Initially hyperplasia is **TSH-dependent** but later becomes **autonomous**.

Types &causes of goiter

Type of Goiter	Cause	Typical Symptoms and Signs
Iodine deficiency (endemic goiter)	Lack of sufficient dietary iodine intake	Thyroid gland enlargement (goiter) Normal or underactive thyroid (hypothyroidism)
Graves disease (diffuse toxic goiter)	Autoimmune stimulation of the thyroid gland	Goiter Hyperthyroidism
Autoimmune thyroiditis (Hashimoto, chronic lymphocytic)	Persistent immune system inflammation of person's own thyroid	Goiter Hypothyroidism
Subacute thyroiditis (painful, de Quervain)	Viral infection	Painful, tender and swollen gland Malaise, fever, chills, and night sweats Thyrotoxicosis, often followed by hypothyroidism
Toxic adenoma and toxic multi-nodular goiter	Benign thyroid tumor(s)	Nodular goiter Hyperthyroidism
Goiter and thyroid nodules suspicious for malignancy	Malignant thyroid tumors	No symptoms Local neck symptoms Symptoms of tumor spread

Table1; shows most of types &causes of goiter

Causes

The different etiologic mechanisms that can cause a goiter include the following:

- Iodine deficiency
- Autoimmune thyroiditis - Hashimoto or postpartum thyroiditis
- Excess iodine (Wolff-Chaikoff effect) or lithium ingestion, which decrease release of thyroid hormone
- Goitrogens
- Stimulation of TSH receptors by TSH from pituitary tumors, pituitary thyroid hormone resistance, gonadotropins, and/or thyroid-stimulating immunoglobulins
- Inborn errors of metabolism causing defects in biosynthesis of thyroid hormones
- Exposure to radiation
- Deposition diseases
- Thyroid hormone resistance
- Subacute thyroiditis (de Quervain thyroiditis)
- Silent thyroiditis
- Riedel thyroiditis
- Infectious agents
- Acute suppurative - Bacterial
- Chronic - Mycobacteria, fungal, and parasitic
- Granulomatous disease
- Thyroid malignancy
- Low selenium levels: This may be associated with goiter prevalence.

Non toxic goiter

Causes:

1. Iodine deficiency
2. Dietary goitrogens
3. Hashimotos Thyroiditis
4. Subacute Thyroiditis
5. Dyshormononogensis
6. Neoplasm : benign or malignant

Iodine deficiency:

- Most common cause of endemic goiter.
- Daily allowance 150-300 ugm/day.

Dietary goitrogens:

- Rare cause of goiter.
  1. Most common is iodide itself (especially in susceptible individuals and hypothyroidism).
  2. Lithium carbonate
  3. Amiodarone
  4. Some vegetable foodstuffs: **goitrogens** found in certain roots and seeds Cyanogenic glycosides found in cassava and cabbage→ release thiocyanates→goiter.

Compounds as phenols, phthalates, pyridines, polyaromatic hydrocarbons found in industrial waste water… all these are weakly goiterogenic (endocrine disruptors**).**

Hashimoto Thyroiditis:

- Most common cause of goiter in developed countries.
- Subacute Thyroiditis: causes goiter and exquisite tenderness.

Dyshormonogensis (familial goiter):

(a)Complete form: cretin with goiter

(b) Incomplete form: mild hypothyroidism with goiter.

C/P

- Mass.
- Pressure symptoms in the neck or thoracic inlet syndrome (with retro sternal extension)
- Recurrent laryngeal nerve paralysis with vocal cord paralysis.
- Hypothyroid symptoms.

Lab. Findings:

Normal TSH, with low or normal free T4.

Radio iodine uptake may be low, normal or high (depending on Iodide pool and TSH derive)

Imaging study:

Hot and cold nodules.

U/S: solid and cystic changes.

DD:

Mainly to rule out malignancy

Treatment:

- Suppressive thyroxine therapy.

Surgery: in suspicious, large with pressure symptoms, RSE

Thyrotoxicosis

Prof. Nagy Shaaban

Clinical syndrome that results when tissues are exposed to high levels of circulating thyroid hormones.

Causes:

1. Diffuse toxic goiter (Graves disease)
2. Toxic adenoma (Plummer disease)
3. Toxic multi-nodular goiter
4. Subacute thyroiditis
5. Silent thyroiditis
6. Thyrotoxicosis factitia
7. Rare causes include: ovarian Struma, metastatic thyroid carcinoma, hydatiform mole, TSH-Producing pituitary tumor

Graves' disease

- Most common cause of thyrotoxicosis
- Female to male incidence 5:1
- Peak incidence 20-40 years
- Consists of: thyrotoxicosis, goiter, ophthalmopathy, dermopathy.

Etiology

- Auto immune disease of unknown cause
- Strong familial predisposition.
- Environmental factors may trigger the process e.g. stress, tobacco use, infection and iodine exposure.
- T-lymphocytes are sensitized to antigen within the thyroid gland → stimulate B lymphocytes → thyroid stimulating antibody (TSAB) or thyroid- stimulating immunoglobulin (TSI) → stimulate thyroid growth and function.

Ophthalmopathy:

Cytotoxic lymphocytes and cytotoxic antibodies are sensitized to antigens in orbital fibroblasts and muscles → ↑ cytokines → proliferation of orbital fibroblasts and orbital tissue → ↑ amount of orbital fat, glycosamino-glycans and inflammation of extraoccular muscles → manifestations of ophthalmopathy.

Dermopathy (pretibial myxedema)

Similar process lead to activation of dermal fibroblasts in the anterior aspect of the legs.

Clinical features of thyrotoxicosis

1. **General features:**
   - Weight loss associated with increased appetite
   - Emotional lability
   - Anxiety and difficult concentration
   - Fatigue due to disturbed sleep

Associated autoimmune diseases:

Pernicious anemia, type I diabetes, RA, myasthenia gravis, vitiligo, adrenal insufficiency

Thyroid:

Diffuse, painless and firm enlargement of the thyroid

2. **Neurologic features**
   - Fine tremors in the hands
   - Proximal muscle weakness → difficulty in climbing stairs, reach the arm over the head, standing from the sitting position.
3. **Dermatologic features:**
   - ↑ sweating, skin is worm, soft and smooth
   - Heat intolerance
   - Fingernails are separated from the nail bed (onycholysis)
   - Pretibial myxedema occurs in a small subset of patients with Graves's disease. It is characterized by lymphocyte infiltration of the dermis, accumulation of glycoaminoglycans, and edema. It occurs in the anterolateral aspect of the shin. The skin is thickened, indurated and non-pitting. It may be pruitic or painful
   - Clubbing of fingers may occur (thyroid acropachy)

4. **Ophthalmologic features**
   - Lid lag and stare look: due to ↑ sympath. tone → contraction of the eyelid muscles (Muller muscle)
   - Proptosis (exophthalmos): due to ↑ in volume of retro-bulbar tissue
   - Diplopia and limitation of eye movements at one or more gaze due to involvement of extraoccular muscles
   - Dry or gritty sensation of the eye and corneal ulceration due to inability to fully close the eye lids.
   - Other complications include peri-orbital edema, conjunctival edema and hyperemia and photophobia.

5- Cardiovascular

- ↑ in heart rate, wide pulse pressure
- Flow murmur over precordium
- Cardiac arrhythmia: atrial fibrillation, multiple premature beats
- CHF
- Anginal attacks

6- Gastrointestinal:

- Hyperphagia associated with weight loss
- ↑ gut motility → frequent defecation and/or diarrhea
- Obstructive dysphagia when large goiter is present

7- Reproductive system:

- Menstrual irregularities specially oligomenorrhea.
- Gynecomastia and sexual dysfunction: ↑ SHBG which has higher affinity to androgens → ↓ level of free androgens relative to estrogens. Also there is ↑ aromatization of testosterone to estrogens in the peripheral tissues.

8- Bone:

- ↑ Thyroid hormone → ↑ loss of cortical and trabecular bone → ↑ risk of osteoporosis and bone fractures.

Lab findings:

- ↓ TSH concentration
- ↑ free T4 and T3
- T3 level only may be ↑ in some cases (T3 toxicosis)
- ↑ in TSAb
- Hyperglycemia due to ↑ in catecholamine – induced glycogenolysis.
- Hypercalcemia and ↑ in alkaline phosphatase due to ↑ bone resorption.

Thyroid scintigraphy:

- Use technetium or iodine 123
- It shows diffuse uptake of radioisotope by thyroid.

Treatment of Graves Disease

A- Anti-thyroid drugs:

- Methimazole, carbimazole and propylthiouracil (PTU)
- They inhibit thyroid hormone synthesis

- PTU also prevent peripheral conversion of T4 to T3.

Recommendation

1. Thyroid function should be checked every 4-6 weeks and doses are adjusted to achieve and maintain euthyroid state and avoid hypothyroidism.
2. Focus on free T3 and T4 level to assess thyroid state because TSH may be suppressed for several months after peripheral thyroid hormone levels are normalized.

Duration of therapy

- 1-2 years to offer a chance for remission of hyperthyroid state.
- The chance of permanent remission after cassation of therapy is 35%-50%.

Dose and regimens:

- Start with large dose. When the patient becomes eurthryoid after 4-12 weeks, maintenance therapy is achieved with lower dose.
- For methimazole start with 10-20 mg/day and maintain with 5-10 mg/day
- For PTU start with 300 – 400 mg/day and maintain with 50-200 mg/day.
- Another approach is to continue large loading dose and add thyroid hormone (block and replace therapy)

Indications:

1. Mild disease and small goiter because they have high chance of remission
2. Elderly or other comorbidities increasing surgical risk.
3. Limited life expectancy
4. previous operation or irradiation to the neck
5. Lack of high-volume thyroid surgeon

Side effects

1. Skin rash, arthralgia, GI problems
2. Agranulocytosis: Potentially lethal adverse effect presents with fever, sore throat which progress to sepsis. Any patient on thionamide therapy who present with fever and sore throat should have complete blood picture to exclude this condition.
3. **Hepatic problems**
   - Methimazole may produce cholestasis
   - PTU may produce hepatitis with elevated markers of hepatocellular injury.

- Patients on thionamide therapy should have liver function before starting therapy and during treatment with antithyroid drugs.

B- Radio-active iodine

- Suitable for most patients with Graves' disease.
- It is effective, safe, and does not require hospitalzation.
- Given orally in a single dose in a capsule or liquid form.
- Very few side effects as no other tissue absorb RAI.

Precautions:

Patients with severe hyperthyroidism, elderly patients or patients with underlying heart disease should be pretreated with anti-thyroid drugs and β-blockers to achieve an euthyroid state prior to radio-active iodine.

Indication:

1. ↑ surgical risk due to associated comorbidities.
2. Previous operation or irradiation to the neck
3. Lack of access to high-volume thyroid surgeon
4. Contraindication for use of anti-thyroid drugs.

Disadvantages:

- Occurrence of permanent hypothyroidism
- Worsening of ophthalmopathy via unknown mechanism.

Contraindication:

- Pregnancy and lactation.
- Children
- Associated severe opthalmopathy

C- Thyroidectomy is indicated in:

- Failure of response to anti-thyroid drugs.
- Severe adverse reactions to anti-thyroid drugs.
- Patient refuses radioactive iodine treatment.
- Huge goiter which cause pressure symptoms.
- Suspected malignancy in thyroid gland.

Preoperative preparation:

- Anti-thyroid drugs to reduce hyperfunction.
- β-blockers to control pulse rate below 80/min.
- Potassium iodide may be given for 2 weeks before surgery. It reduce intraoperative blood loss.

Complications

A. Hypothyroidism.

B. Risk of hypoparathyroidsm.
C. Recurrent laryngeal nerve damage.
D. Complications of general anesthesia.

D-Adjuvant therapy (β-blockers)

Should be given to:

- All thyroid patients with resting heart rate >90/min.
- Elderly patients with symptomatic thyrotoxicosis.

Toxic multi-nodular goiter

Etiology:

- Occur in patients with long-standing multi-nodular goiter.
- There is constitutive activation of TSH receptors in thyroid nodules due to mutation in TSH receptor gene.

Clinical picture:

- Nodular thyroid enlargement.
- Manifestations of thyrotoxicosis.
- No opthalmopathy or dermopathy

Thyroid scintigraphy:

Heterogenous pattern with areas of hyperactivity (hot areas) interspersed with hypoactive regions.

Treatment:

- Radioactive iodine
- Surgery (thyroidectomy) if the goiter is large and cause pressure symptoms.

Toxic solitary nodule

Autonomous function nodule that produces excessive amount of thyroid hormones.

Etiology:

Constitutive activation of TSH receptors due to mutation in TSH receptor gene.

Clinical picture:

- Solitary thyroid nodule.
- Mainfestations of thyrotoxicosis.
- No opthalmopathy or dermopathy

Thyroid scintigraphy:

Hyperactive (hot) area, the rest of the gland is hypoactive because TSH is suppressed by excessive thyroid hormones.

Treatment:

Radio-active iodine

Surgery: if the nodule is large and cause pressure symptoms.

Sub acute and silent thyroiditis

Clinical picture:

- Pain in the neck.
- Tender thyroid gland.
- Mild to severe thyrotoxicosis due to acute release of T4 and T3 into circulation from destructed thyroid follicles.
- Symptoms subside spontaneously over a period of weeks or months.

Thyroid scintigraphy

- No RAIU

Treatment:

- Anti-thyroid drugs has no role because there is no ↑ in thyroid hormone synthesis.
- Symptomatic treatment.

Thyrotoxicosis factitia

Etiology:

Ingestion of large doses of T4 or thyroid hormone preparation usually for the purpose of weight control.

Clinical picture:

- Manifestations of thyrotoxicosis.
- No goiter
- No opthalmopathy or dermopathy.

Thyroid scintigraphy:

- RAIU is markedly decreased.

Thyrotoxic Crisis

Definition: Thyrotoxic crisis also referred to as thyroid storm, is an acute, rare life-threatening, hypermetabolic state induced by excessive release of thyroid hormones in individuals with thyrotoxicosis. It is an endocrinal emergency.

Cause:

- Thyroid storm is precipitated by the following factors in individuals with thyrotoxicosis:
- Stress
- Sepsis in untreated patients
- Surgery with lack of preoperative preparation

- Anesthesia induction
- Radioactive iodine (RAI) therapy
- Drugs : anticholinergic and adrenergic drugs such as pseudoephedrine, salicylates; nonsteroidal anti-inflammatory drugs [NSAIDs], chemotherapy and iodinated contrast agents
- Diabetic ketoacidosis
- Excessive thyroid hormone ingestion
- Withdrawal of or noncompliance with anti-thyroid medications
- Direct trauma to the thyroid gland
- Vigorous palpation of an enlarged thyroid
- Toxemia of pregnancy and labor in older adolescents; molar pregnancy

Clinical picture:

- History: patients may have a known history of thyrotoxicosis.
- General symptoms: hyperpyrexia, sweating, weight loss and fatigue
- GIT :nausea, vomiting, diarrhea, Jaundice and aute abdominal pain
- CNS :anxiety altered behavior, seizures, coma, in old age apathy and bulbar symptoms from myopathy
- CVS: tachycardia, Cardiac arrhythmia as supraventricular arrhythmias are more common, but ventricular tachycardia may also occur, acute high-output heart failure, hypertension with wide pulse pressure and later hypotension

➢ Thyroid storm may be the initial presentation of thyrotoxicosis in undiagnosed children, particularly in neonates.

➢ Clinical picture may be masked by B-blockers

Differential Diagnoses

- Heart Failure
- Arrhythmia
- Hypertension
- Pheochromocytoma
- Neurosis

Management: emergency

Patients with thyroid storm should be treated in an ICU setting for close monitoring of vital signs and invasive monitoring and inotropic support.

a- Anti-thyroid:

- Propylthiouracil: 200-400 mg/8h. (orally,rectally or nasogstric).

- Propranolol in full dose is started immediately for tachyrrhthmias (160 mg/d orally or 1 mg/4h IV)
- Na iodide or K iodide: 1 gm over 24h to ↓ release of thyroid hormones.
- Hydrocortisone: 100 mg/8h IV or IM to ↓ release of T4 & ↓ conversion of T4 to T3 and to correct hypotension

➢ Thyrotoxic crises →↑↑ cortisol metabolism →relative adrenal insufficiency →refractory hypotension.

B- Symptomatic:

- Antipyretics : ice bags and acetaminophen
- IV fluids for dehydration:
- Digoxin and diuretics for AF& HF
- Nasogastric tube for bulbar palsy, nausea and vomiting

c- Ttt of cause & ppt factors: e.g. antibiotics for infection

Struma ovarii (ovarian struma)

Etiology:

Teratoma of the ovary which contain hyperactive thyroid tissue.

Clinical picture:

- Mild thyrotoxicosis
- No goiter
- No opthalmopathy or dermopathy.

Thyroid scintigraphy:

- ↓ RAIU
- Total body scan reveals uptake of radioiodine in the pelvis.

Thyroid carcinoma

- Follicular thyroid carcinoma rarely secretes thyroid hormones.
- Metastatic thyroid cancer rarely present with thyrotoxicosis.

TSH- Producing Pituitary Tumor

Etiology:

- TSH- producing macroadenoma of the pituitary.

Clinical picture:

- Rare.
- Mass effect of the pituitary tumor
- Mild thyrotoxicosis.

Investigation:

- Elevated T4, T3.
- Inappropriate elevation of TSH or within the normal range.

Amiodarone induced thyrotoxicosis

Amiodarone is an anti arrhythmic drug which contains large amount of iodine.

Etiology:

↑ Synthesis and secretion of thyroid hormone by underlying multi-nodular or diffuse goiter → thyrotoxicosis.

Amiodarone induced thyroiditis → release of preformed hormones from damaged and inflamed thyroid gland.

Clinical picture:

Thyrotoxicosis.

Treatment:

- Stop amiodarone
- Antithyroid drugs for the first category
- Corticosteroid for the second catergory

Hypothyroidism

Definition:

- It is a clinical and biochemical syndrome with manifestations of thyroid hormone deficiency at target tissues.

Epidemiology:

- Prevalence is 4-8% of general population.
- Female to male ration is 3:1

Causes:

- Post Thyroiditis
- Post surgical
- Post radioiodine
- Congenital

Presentation according to age:

- Cretinism: onset at infancy
- Juvenile myxedema: onset before puberty
- Adult hypothyroidism (myxedema): onset after puberty

Cretinism:

- Aplasia or hypoplasia of thyroid tissue
- Metabolic (dyshormonogenesis)
- Iodine deficiency
- Use of anti-thyroid drugs or radio iodine during pregnancy.
- Pendred`s syndrome (congenital hypothyroidism and nerve deafness)

Clinical Picture:

- Subnormal body temperature, poor suckling
- Face: puffy eyes, depressed nasal bridge, macroglossia, thick lips, delayed dentition
- Hands: square shaped
- Disproportionate dwarfism: shorter limbs, upper segment more than lower segment, and height more than the span.
- Muscle weakness: waddling gait, protuberant abdomen, and abdominal hernias
- Epiphyseal dysgenesis with thickening of the growing plates of long bones.
- Skin: dry, rough, scaly, and cold. Deposition of myxomataous tissue particularly in dorsum of hands, supraclavicular fossa and face.

- Mental retardation: mental changes are irreversible if hypothyroid state begins before one and half years, but if later onset, they are reversible.
- Cardiovascular: bradycardia, low voltage and ST-T changes in ECG.

Investigations:

- High serum lipids.
- Epiphyseal dysgenesis on plain X Ray of bones.
- Low thyroid hormones with high TSH.

Screening:

- Screening of umbilical cord (or heel) blood is mandatory for all newly borne whether delivery occurs at hospital or home, because diagnosis of neonatal hypothyroidism may be delayed and thyroid hormones are essential for brain development

Juvenile Myxoedema

- Onset of hypothyroidism in late childhood and before puberty.
- Normal mental functions
- Disproportionate dwarfism
- Epiphyseal dysgenesis
- Delayed puberty or paradoxically sexual precocity.

Adult hypothyroidism (myxoedema)

Causes:

A: Primary thyroid failure, thyroprevic:

- Idiopathic
- Thyroiditis:
- Post thyroidectomy
- Post radioiodine
- Goiterogens

B. Secondary thyroid failure (to pituitary failure) , thyrotrophic:

C. Tertiary thyroid failure: hypothalamic leions

- Sometimes , causes of pituitary and hypothalamic origin are collectively termed " ***central hypothyroidism***"

Clinical manifestations:

- Expressionless apathetic face, with puffy eyes and lost outer third of eye brows hair.
- Malar flush
- Thickened lips and tongue
- Low body temperature with intolerance to cold weather.
- Skin is thick, dry, scaly, pale and coarse.

- Carotenoderma.
- Weakness, fatigue arthralgia and musculoskeletal pains.
- Slow movements and weight gain.

Cardiovascular manifestations:

- Sinus bradycardia and heart block.
- Pericardial effusion (cholesterol pericarditis), less prone to produce hemodynamic compromise.
- Enhanced atherosclerosis, affecting coronaries and peripheral arteries (hypertension, atherogenic lipid profile, and hyperhomocystienemia)
- Myxoedematous heart disease of ischemic and metabolic backgrounds.
- Hypertension especially diastolic due to invreased peripheral resistance.
- Cardiomegaly and congestive heart failure.
- Rarely asymmetric septal hypertrophy (ASH).
- ECG changes: sinus bradycardia, prolonged P-R interval, low volt QRS complexes, ST –T wave changes.

Neurologic manifestations:

- Poor cerebral performance, thinking, memory, and hypersomnia
- Hoarseness of voice, with slurred speech
- Suspended tendon jerks (delayed muscle relaxation)
- Peripheral neuropathy
- Entrapement neuropathy eg. carpal tunnel syndrome.
- Muscle hypertrophy involving gastrocnemius, back, and upper limbs with EMG myopathic changes.
- Myxoedema madness with frank psychosis.
- Myxoedema coma.

Gastrointestinal manifestations:

- Atrophic gastritis with slow gastric motility.
- Atrophic intestinal villi with slow absorption, might lead to steatorrhea.
- Constipation, megacolon and pseudo intestinal obstruction with ileus.
- Ascites.

Reproductive manifestations:

- Menstrual disturbances as menorrhagia or oligomenorrhea.
- Subfertility and anovulation.
- Amenorrhea- galactorrhea syndrome
- Spontaneous abortion

- Pregnancy induced hypertension.
- Gynecomastia in males.

Urogenital:

- Reduced renal plasma flow and glomerular filtration rate.
- Increased total body water.
- Hyponatremia.
- Syndrome of inappropriate secretion of antidiuretic hormone (SIADH).

Respiratory manifestations:

- Dyspnea: due to respiratory muscle weakness, cardiomyopathic, pleural effusion, and pulmonary function abnormalities.
- Sleep apnea: *obstructive* due to macroglossia and enlarged pharyngeal muscles, and *central* component due to reduced ventilatory drive.
- Sinusitis.

Metabolic manifestations:

- Slowing of metabolic processes which results in decreased energy expenditure, oxygen consumption and use of substrate.
- Reduced thermogenesis, decreased appetite, with increased body fat.
- ***Hypercholesterolemia***, high LDL, high lipoprotein (a) and high oxidized LDL. Serum cholesterol can be used as a marker for tissue hypothyroidism i.e. the higher the cholesterol the lower the thyroid hormones.
- Normal triglycerides or modestly elevated.
- Hyperhomocystienemia

Hematologic manifestations:

- Anemia: normocytic normochromic due to reduced erythropoietin levels and low oxygen requirements may be iron deficiency due to blood loss from menstrual troubles, or macrocytic hyperchromic of associated pernicious anemia.
- Normal leucocytes and platelets.
- Bleeding tendency with prolonged bleeding time (thromboathenia and low factor VIII).

Endocrinal manifestations:

- Decreased ***HGH*** secretion due to increased somatostatinergic tone with resulting decrease of IGF-1.
- Moderate ***hyperprolactinemia*** due to high TRH (spill over).
- Wide pituitary fossa due to hyperplasia of pituitary thyrotrophs which rarely cause distinct pituitary adenoma.

- Reduced bone turnover (decreased activity of osteoblasts and osteoclasts).
- Decreased metabolic clearance and production of cortisol, with normal serum cortisol.

Laboratory diagnosis:

- High TSH and low FT4 in primary hypothyroidism.
- Central hypothyroidism has low TSH and low FT4.
- High TSH but normal FT4 diagnose ***subclinical hypothyroidism*.**

Treatment:

- Replacement therapy with oral levothyroxine sodium in a daily dose of 1.6 ugm/kg/day. With average 100-200 ug/day.
- Start with a low dose and gradual titration up depending on severity and duration of hypothyroid state, age of the patient, and presence of heart disease. In severely hypothyroid, elderly, or having ischemic heart, start with low dose and titrate slowly.

Myxedema coma

- It is a rare, life- threatening clinical condition in patients with long standing severe hypothyroidism.

Precipitating factors:

- Cold exposure.
- Infections.
- Drugs: diuretics, sedatives and tranquilizers.
- Trauma.
- Surgery.
- Stroke.
- Heart failure and acute MI.
- GIT bleeding.

Clinical picture:

- The typical patient is elderly woman in winter season.
- Altered thermoregulation with ***hypothermia***.
- Altered central nervous system with disorientation, lethargy, psychosis and coma.
- Altered cardiovascular system: bradycardia and hypotension.

Laboratory diagnosis:

- Low FT4.
- TSH is usually high.
- ***CPK is sky high.***

Treatment:

- Start with ***levothyroxine*** sodium 300-500 ugm IV, then 50-100ugm/daily till oral therapy can be given. LT3 may be combined with LT3.
- ***Hydrocortisone*** IV 100-200 mg daily in divided doses.
- Supportive measures:
- Hypothermia: blankets.
- Hypoventilation: mechanical ventilation.
- Hypotension: whole blood or saline cautiously.
- Hyponatremia: mild fluid restoration.
- Hypoglycemia: glucose IV.

Thyroiditis

Definition: inflammation of the thyroid gland:

Causes and characteristics:

(1) **Acute**: suppurative or pyogenic thyroiditis, which is due to bacterial infection

(2) **Subacute**: (de Quervain s) thyroiditis, which results from a viral infection of the gland: multinuclear giant cells.

(3) **Chronic** (the commonest): autoimmune thyroiditis; Hashimoto s or atrophic: grossly lymphocytic or fibrotic

(4) **Others**:

- Post- partum thyroiditis: lymphocytic.
- Drug- induced thyroiditis (amiodarone, interferon alpha)
- Radiation thyroiditis.
- Riedel s (chronic fibrosing) thyroiditis: extensive fibrosis.

Clinical presentation:

Forms of thyroiditis	Clinical presentation	Thyroid function
Acute: suppurative	Painful, tender thyroid, fever	Usually normal
Subacute: (de Quervain s)	Painful anterior neck, preceding URTI, arthralgia, generalized fatigue.	Early thyrotoxicosis, Occasionally late hypothyroidism.
Autoimmune	Hashimoto s: goiter (painless) Atrophic: no goiter	Usually hypothyroid Sometimes euthyroid Rarely early thyrotoxicosis High titres of antithyroid antibodies
Post-partum	Thyroid dysfunction within the first six month	Transient thyrotoxicosis or hypothyroidism
Riedel s	Hard, woody consistency of thyroid	Usually normal

Thyroiditis

Subacute Thyroiditis

(De Quervain, Acute viral Thyroiditis, Granulomatous Thyroiditis, migrating Thyroiditis):

Def: acute inflammatory condition due to viral infection.

E.g. Mumps, coxcakie, adenovirus

Pathology: inflammatory reaction involving the capsule, destruction of thyroid parenchyma, phagocytes.

C/P: fever, local pain in the neck radiating up .

Symptoms of thyrotoxicosis like sweats, palpitation.

On exam. The gland is exquisitely tender but no redness or hotness (to exclude abscess).

Signs of thyrotoxicity.

Lab: initially toxic profile with low RAIU….then recovery …. Or reach hypothyroid range.

Malignantly high ESR.

Negative thyroid autoantibodies.

Ttt: NSAID
Short course of steroids 20 mg tds for a week.
Prognosis: complete resolution in weeks or months
Hypothyroidism in 10% of cases

Chronic Thyroiditis:
Synonyms: Hashimoto Thyroiditis, chronic immune thyroiditis, **lymphocytic Thyroiditis:**
Is considered the most common cause of hypothyroidism and goiter in developed countries.
Auto immune thyroid spectrum at one end Graves and the other end myxoedema.
Toxic Graves…euthyroid Graves….Hashimoto…idiopathic myxoedema

Pathology: immunologic inflammation with heavy lymphocyte infiltration.
Lymphoid follicles with germinal center may be found. Follicular epithelium may be cytoplasm with basophilic cytoplasm (Hurthle cell).
Antibodies: anti TG
Anti peroxidase TPO (formerly called antimicrosomal)
TSH -receptor blocking Ab.
C/P:
painless condition
Goiter
Hypothyroidsm
Lab: normal or hypothyroid profile.
High titer of thyroid auto antibodies: anti TG, TPO.
FINAC: lymphocyte infiltration with Hurthle cells.

Complications:
Progressive hypothyroidism
Thyroid lymphoma (rare)… rapid growth inspite of T4 replacement… diagnosed by surgical biopsy
Prognosis:
Goiter,
Hypothyroidism.
May develop Graves (**Hashitoxicosis**) with GRO and dermopathy….Hashimoto blunt the toxic manifestations of Graves = euthyroid Graves
Differential diagnosis:
(1)- Other causes of hypothyroidism.

(2)- Other causes of hyperthyroidism.

Treatment:

Acute: suppurative: Antibiotic therapy and incision and drainage if fluctuant area within the thyroid should occur.

Subacute: (de Quervain`s): non- steroidal anti-inflammatory agents and paracetamol in mild cases.

In severe cases, glucocorticoids can be effective. Propranolol can be used to control associated thyrotoxicosis. T4 replacement is required if the patient is hypothyroid.

Autoimmune thyroiditis: T4 replacement in hypothyroid patients.

Post- partum thyroiditis: most patients have a complete remission but some may progress to permanent hypothyroidism and need for replacement.

Thyroid carcinoma

Types:

type	frequency	behavior	prognosis
1- papillary	70%	Slowly growing, occurring in young people.	Good
2- follicular	20%	Commoner in females	Good if resected
3-anaplastic	<5%	Aggressive	Very poor
4-lymphoma	<2%	variable	May respond to radiotherapy
5- medullary	5%	From parafollicular (C) cells, secrete calcitonin, often familial.	poor

Etiology:

1- Neck irradiation papillary carcinoma.

2- MNG follicular carcinoma.

3- Hashimoto thyroiditis malignant lymphoma.

4- Genetic element Cowden syndrome (well differentiated thyroid cancer & breast cancer & multiple hematomas).

Clinical picture:

Symptoms: the patient may be present by one of the following:

1- **Long standing goiter** then recent rapid increase in size, become painful & the pain is referred to the ear (along the auricular branch of vagus),

invasive symptoms (progressive hoarseness, dysphagia, dyspnea &hemoptysis).
2- **Goiter of recent onset** but rapidly growing with pressure & infiltration symptoms.
3- **Solitary thyroid nodule** (hard, fixed, >1cm)
4- **Occult presentation:** the pt present by lymphatic or haematogenous metastasis before the 1ry tumor is discovered (e.g. lateral aberrant thyroid in papillary carcinoma).
5- **Thyrotoxicosis** with functioning follicular carcinoma or diarrhea 30% with medullary carcinoma (due to production of PGs or 5 hydroxytyrptamine).

Signs:

a- general examination: for manifestation of metastasis.

b- Local examination:

 Thyroid lump: hard, fixed (to the skin, trachea or sternomastoid may infiltrate the carotid sheath loss of carotid pulsation (berr`s sign).
 CX LNS: enlarged >1cm, hard, fixed, not tender.

Investigation:

a- for the 1ry tumor:

- Laboratory:

1- Thyroid function tests.
2- Tumor markers:
 S.thyroglobulin: increase in differentiated thyroid carcinoma & decrease after resection, if increase again recurrence.
 S.calcitonin: increase in medullary carcinoma.

- Radiological:

 Thyroid scan: cold nodule
 Neck U/S: site, size &nature of the lesion (solid or cystic)
 CT &MRI
 Plain X-ray: punctate calcification, tracheal shift, retrosternal extension.

- Endoscopic: indirect laryngoscopy for cord mobility

-biopsy

 FNAC
 true-cut needle biopsy.
 Open surgical biopsy.

b- for 2ry: metastatic work up e.g. bone survey, chest x-ray, abd.U/S ... etc

Treatment:

1- When possible, thyroid carcinoma is treated surgically.

2- **131I** therapy is of value if the carcinoma takes up the isotope (only papillary and follicular types). If the pt had a subtotal thyroidectomy, remaining thyroid tumor is ablated with high dose of **131I**. Replacement therapy is then given for 6 weeks. it is then stopped to allow TSH level to rise followed by giving an ablative dose of **131I** to treat metastasis or persistent local disease .this may be repeated 3-4 monthly as long as isotope scans show persistent metastatic or local disease .the measurement of thyroglobulin in plasma may be used as a tumor marker . Levels above 10ug/l indicate a high chance of remaining disease.

3- Tumors which do not take up I are treated by radiotherapy to the local tumor.

4- in medullary carcinoma, the patient`s family should be screened for this tumor and other endocrine malignancies.