HYPERTHYROIDISM

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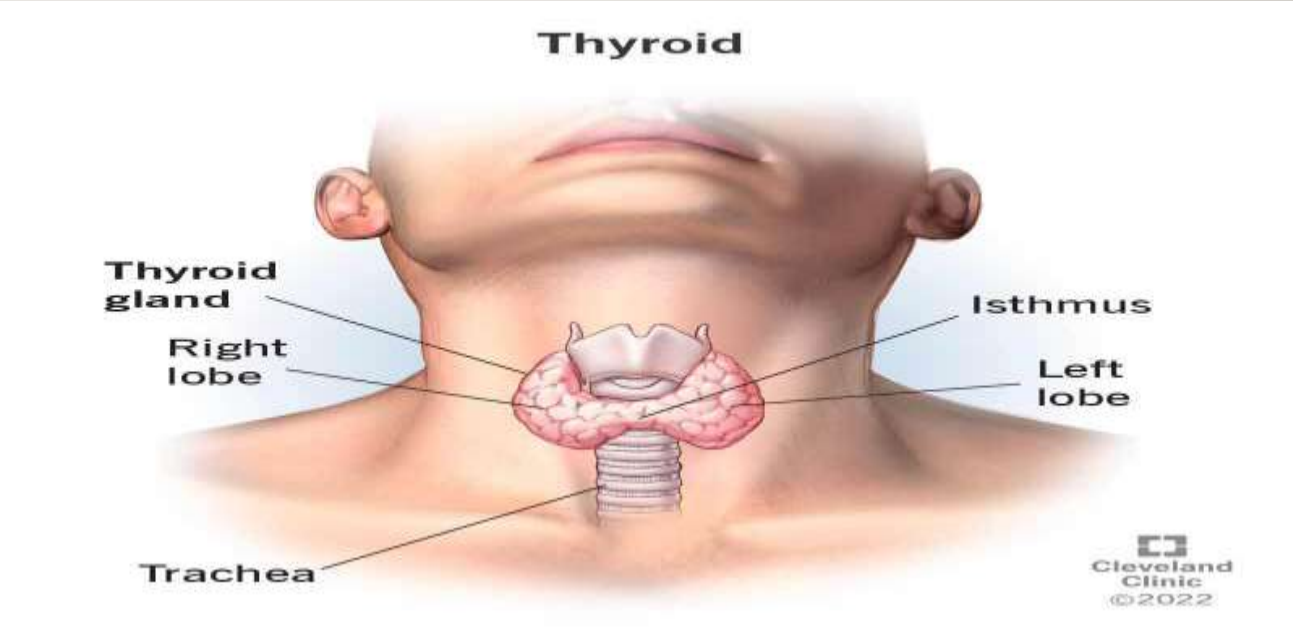
7
21st Batch

THYROID GLAND

- Thyroid gland is one of the largest endocrine gland in the body, and consists of two connected lobes.
- It is found in the anterior neck, below the laryngeal prominence



- Diseases of the thyroid affect 5% of the population, predominantly females
- Follicular epithelial cells synthesize thyroid hormones by incorporating iodine into the amino acid tyrosine.
- The thyroid secretes predominantly thyroxine (T4) and only a small amount of triiodothyronine (T3), the more active hormone; ~85% of T3 in blood is produced from peripheral conversion of T4.
- They both circulate in plasma almost entirely (> 99%) bound to transport proteins, mainly thyroxine-binding globulin(TBG)
- The unbound hormones diffuse into tissues and exert diverse metabolic actions.

- Production of T3 and T4 in the thyroid is stimulated by thyroid stimulating hormone (TSH), a glycoprotein released from the thyrotroph cells of the anterior pituitary in response to the hypothalamic tripeptide thyrotrophin-releasing hormone (TRH).

- There is a negative feedback of thyroid hormones on the hypothalamus and pituitary such that in thyrotoxicosis, when plasma concentrations of T3 and T4 are raised, TSH secretion is suppressed.

- Conversely, in primary hypothyroidism, low T3 and T4 are associated with high circulating TSH levels.

HYPERTHYROIDISM

- Hyperthyroidism is a set of disorders that involve excess synthesis and secretion of thyroid hormones (T3 and T4) by the thyroid gland, which leads to the hypermetabolic condition of thyrotoxicosis.

THYROTOXICOSIS

- **Thyrotoxicosis refers to the clinical manifestations arising from elevated circulating levels of thyroid hormone.**
- **Common causes include:**
  - **Graves' disease**
  - **Multinodular goitre**
  - **Autonomously functioning thyroid nodules (toxic adenoma)**
  - **Thyroiditis**

i 20.6 Causes of thyrotoxicosis and their relative frequencies

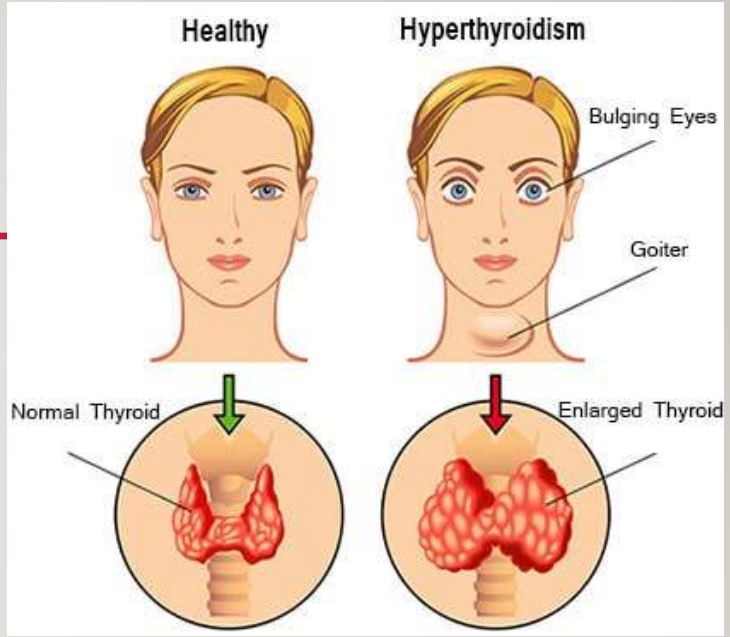
Cause	Frequency[1] (%)
Graves' disease	76
Multinodular goitre	14
Solitary thyroid adenoma	5
Thyroiditis	
Subacute (de Quervain's)[2]	3
Post-partum[2]	0.5
Iodide-induced	
Drugs (amiodarone)[2]	1
Radiographic contrast media[2]	–
Iodine supplementation programme[2]	–
Extrathyroidal source of thyroid hormone	
Factitious thyrotoxicosis[2]	0.2
Struma ovarii[2,3]	–
TSH-induced	
TSH-secreting pituitary adenoma	0.2
Choriocarcinoma and hydatidiform mole[4]	–
Follicular carcinoma±metastases	0.1

[1]In a series of 2087 patients presenting to the Royal Infirmary of Edinburgh over a 10-year period. [2]Characterised by negligible radioisotope uptake. [3]i.e. Ovarian teratoma containing thyroid tissue. [4]Human chorionic gonadotrophin has thyroid-stimulating activity.
(TSH = thyroid-stimulating hormone)

CLINICAL FEATURES

- **Symptoms**:
  - Weight loss with a normal or increased appetite
  - Heat intolerance
  - Palpitations
  - Tremor
  - Irritability

- **Signs**:
  - Tachycardia
  - Palmar erythema
  - Lid lag



- **Goitre**:
  - **Not all patients will have a palpable goitre.**
  - **Graves' disease: Diffuse, soft goitre.**
  - **Multinodular goitre: Irregular enlargement of the thyroid.**

INVESTIGATION

- **Initial Blood Tests:**
  - Serum T3, T4, and TSH levels.
  - Confirm abnormal values if necessary (repeated testing).

- **Typical Results:**
  - Elevated T3 and T4 (with T4 being near the upper range).
  - In T3 toxicosis, T3 is significantly raised.

  - **TSH: Undetectable in primary thyrotoxicosis (may be elevated in secondary thyrotoxicosis due to TSH-producing pituitary adenoma).**

- **TSH Receptor Antibodies (TRAb):Elevated in Grave's disease.**

- Anti thyroid peroxidase (anti-TPO)antibody – significantly elevated in Grave's disease

- **Radioactive Isotope Scanning:**
  Radioactive iodine uptake or ^{99}Tm uptake
  Low uptake suggests thyroiditis.
  High uptake in Graves' disease, toxic nodules, etc.

MANAGEMENT

- **Medical Treatment**:
  - **Antithyroid drugs** (e.g., methimazole,carbimazole, propylthiouracil).side effect : **agranulocytosis**
  - **Radioactive iodine therapy** or **surgery** depending on the cause.
- **Symptomatic Treatment**:
  - **β-Blockers** (e.g., propranolol) to alleviate symptoms like tachycardia, tremor, and irritability.
  - **Dosing**: 160 mg daily of propranolol (short-term use).
  - **Alternative**: **Verapamil** for patients with asthma (primarily for tachycardia).
- **Role of β-Blockers**: Only for short-term symptom management, not long-term treatment.
- **Long-term management** may involve further therapies like radioactive iodine or surgery if necessary.

SUBCLINICAL HYPERTHYROIDISM

- **Subclinical hyperthyroidism** is a condition characterized by:
  - Low or undetectable **TSH** levels.
  - Normal levels of **T3** and **T4**.
- It is a form of thyroid dysfunction that occurs without obvious clinical symptoms of hyperthyroidism.

MANAGEMENT

- **Observation:** In asymptomatic patients, regular monitoring of thyroid function (TSH, T3, T4) is recommended, typically every 6-12 months.

- **Treatment Indications**:
  - If symptoms develop (e.g., palpitations, fatigue) or if there are risks of cardiovascular disease (e.g., atrial fibrillation), treatment is recommended.
  - Treatment is particularly considered in older adults or patients at risk for bone loss or progression to overt hyperthyroidism.

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Treatment Options:

Thyroid hormone adjustment (for those on replacement therapy).

Antithyroid medications (methimazole or PTU) for underlying causes like Grave's disease.

Radioactive iodine or **surgery** for toxic nodules or persistent cases.

Long-term Management: Regular monitoring and addressing **cardiovascular** and **bone health** risks are crucial for managing subclinical hyperthyroidism

GRAVES DISEASE

- **Affects all ages**, but uncommon before puberty; most common in women aged **30-50 years**.
- **Primary manifestation: Thyrotoxicosis** (with or without a diffuse goitre).
- Extrathyroidal features include **ophthalmopathy** and **pretibial myxoedema** (in some cases, even without thyroid dysfunction).

PATHOPHYSIOLOGY

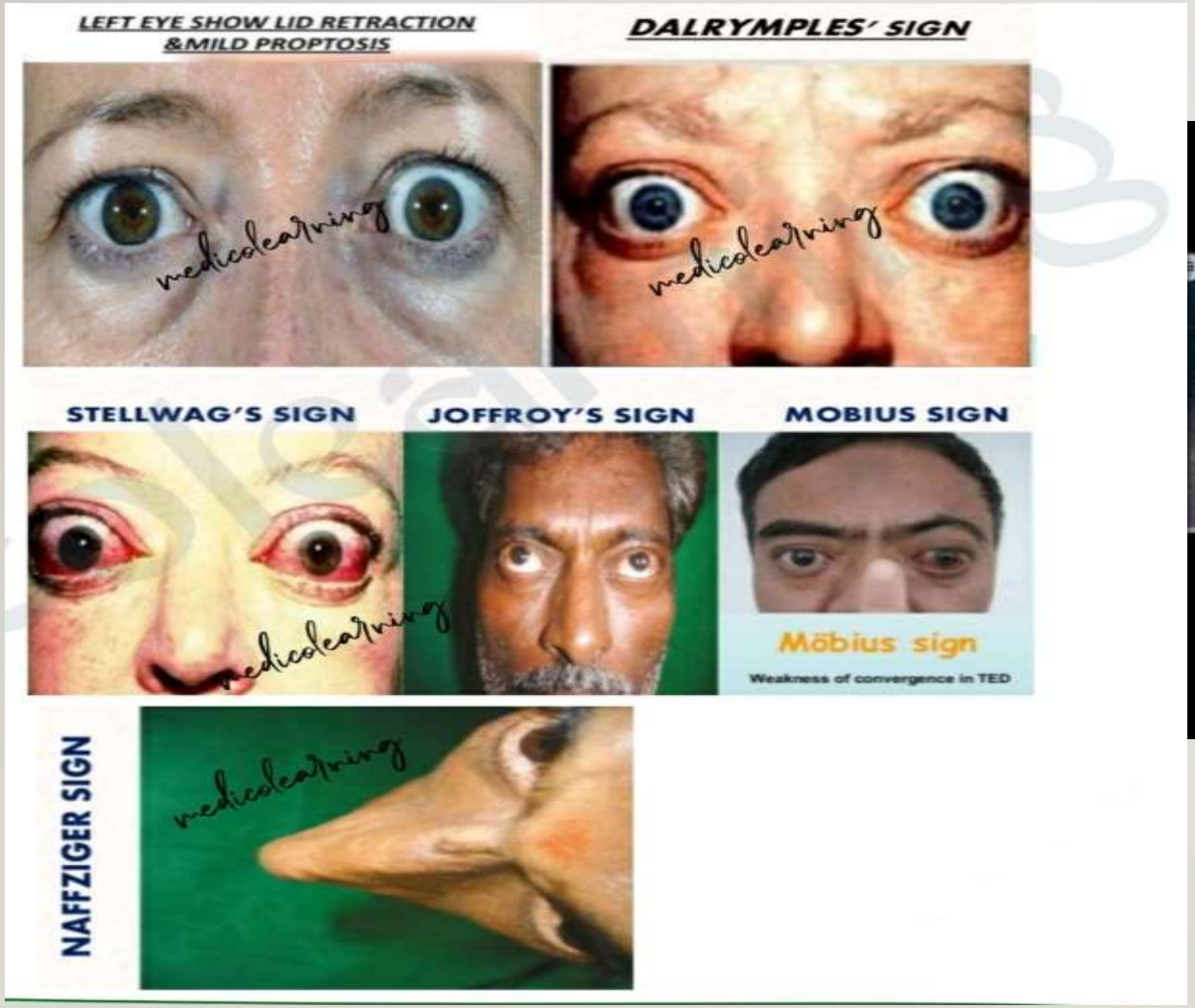
- **Autoimmune disease**: IgG antibodies (TSH receptor antibodies, TRAb) stimulate thyroid hormone production.
- TRAb is present in **>95% cases of Graves' disease**
- **Genetic component**: 20%-40% concordance in monozygotic twins; less than 5% in dizygotic twins.
- **Genes** implicated:**HLA on chromosome 6** (HLA-DR**B1*08 and DRB3*0202)**,certain alleles of CTLA4, TSHR1, CD25, CD40.
- **Environmental triggers**: Infections, iodine supplementation in iodine-deficient areas, and smoking.

CLINICAL FEATURES

- **Thyrotoxicosis**: Weight loss, heat intolerance, palpitations, tremor, irritability.
- **Goitre** : Diffuse enlargement.
- **Ophthalmopathy**: Lid lag(von Graefe's sign) , exophthalmos, diplopia, conjunctival irritation.
- **Pretibial myxoedema** and **thyroid acropachy** (rare).

EYE SIGNS OF THYROTOXICOSIS

- **Dalrymple sign** – rim of sclera is seen all around cornea on looking straightforward
- **Rosenbach's sign** – fine tremor of upper eyelid on slight closure of eye
- **Joffroy's sign** – lack of wrinkling of forehead when looking upward
- **Von Graefe's sign** – lagging upper eyelid on looking downward without moving head
- **Stellwag's sign** – staring looking with frequent blinking
- **Ballet sign** – restriction of one or more extraocular muscles
- **Kocher sign** – staring look (upper sclera visible)


LEFT EYE SHOW LID RETRACTION &MILD PROPTOSIS
DALRYMPLES' SIGN
STELLWAG'S SIGN
JOFFROY'S SIGN
MOBIUS SIGN
Möbius sign
Weakness of convergence in TED
NAFFZIGER SIGN


von GRAEFE SIGN(RIGHT EYE)

MANAGEMENT

- **Symptom Control**: Beta-blockers (e.g., propranolol) for tachycardia and tremors.
- **Definitive Treatment**:
  - **Antithyroid drugs**: **Carbimazole** or **propylthiouracil**.
  - **Radioactive iodine therapy (^{131}I)**
  - **Thyroid surgery**: Considered if other treatments fail.

ANTITHYROID DRUGS

- **Carbimazole (40-60 mg daily)** or **propylthiouracil (400-600 mg daily)** inhibit thyroid hormone synthesis.
- **Side effects**: Rash, agranulocytosis (rare but serious), hepatotoxicity (with propylthiouracil).
- **"Block and replace" regimen**: Carbimazole + levothyroxine (for patients with fluctuating T3/T4 levels).

RADIOACTIVE IODINE (^{131}I)

- Administered as a single oral dose (400–600 MBq), effective in **75% of cases**.
- **Risks**: Can lead to **hypothyroidism** in most cases.
- **Avoid in active Graves' ophthalmopathy** (use with caution and steroids if required).
- **Post-treatment precautions**: Avoid pregnancy for **6 months**, use contraception in men for at least **4 months**.

THYROTOXIC CRISIS/THYROID STORM

- **Thyroid storm** is a **rare, life-threatening** complication of **hyperthyroidism**, characterised by an **acute exacerbation** of symptoms
- It is a **medical emergency** with a high mortality rate if untreated.

CAUSES

- **Graves' disease** (most common cause)
- **Thyroiditis**
- **Excessive thyroid hormone replacement** (over-treatment of hypothyroidism)
- **Thyroid surgery or trauma**
- **Infection** (especially in patients with undiagnosed hyperthyroidism)
- **Postpartum thyroiditis** and **pregnancy-related thyroid conditions**

CLINICAL FEATURES

- **Hyperthermia** (fever > 38.5°C or 101.3°F)
- **Tachycardia** (heart rate > 140 bpm)with **AF, high pulse pressure, hypotension**
- **Altered mental status** (delirium, agitation, confusion, psychosis, or coma)
- **Profuse sweating**, **diarrhea**, and **nausea**
- **Heart failure** (due to increased cardiac output demands)
- **Jaundice** in severe cases

DIAGNOSIS

- **Clinical diagnosis** based on severe **hyperthyroid symptoms**.
- Laboratory findings:
  - **Elevated free T3** and **T4** levels
  - **Suppressed TSH**
  - **Electrolyte disturbances** (e.g., low sodium)
- **Exclusion of other conditions** (e.g., infections, sepsis) is necessary.

MANAGEMENT

- **Immediate supportive care:**
  - Intravenous fluids to correct dehydration and electrolyte imbalances.
  - Cooling measures (antipyretics acetaminophen and cooling blankets).
- **Beta-blockers** : Propranolol 60-80mg orally 4-6 hours or 1-5 mg IV 4 times daily to control tachycardia and hypertension. (atenolol or metoprolol cardio selective)
- **Antithyroid medications** : PTU (propylthiouracil) 200mg orally 4 hourly or methimazole 20 mg orally 4-6 hou carbimazole 15-30 mg stat followed by 15 mg TID to inhibit thyroid hormone synthesis.

Steroids :IV Hydrocortisone 100 mg 8 hourly to decrease the conversion of T4 to T3 and manage adrenal insufficiency.

Iodine therapy : Lugol's Iodine or potassium iodide 10 drops TID given after antithyroid drugs to inhibit hormone release, usually 1 hour after antithyroid drugs are given.

Treatment of precipitating factors:

- Antibiotics if infection is the trigger.
- Heart failure management if needed. (Digoxin)

THANK YOU

Reference:

Davidson principle and practices of medicine 24th edition

ARCHITH BOLOOR 4TH EDITION

MANIPAL MANUAL OF MEDICINE 3RD EDITION