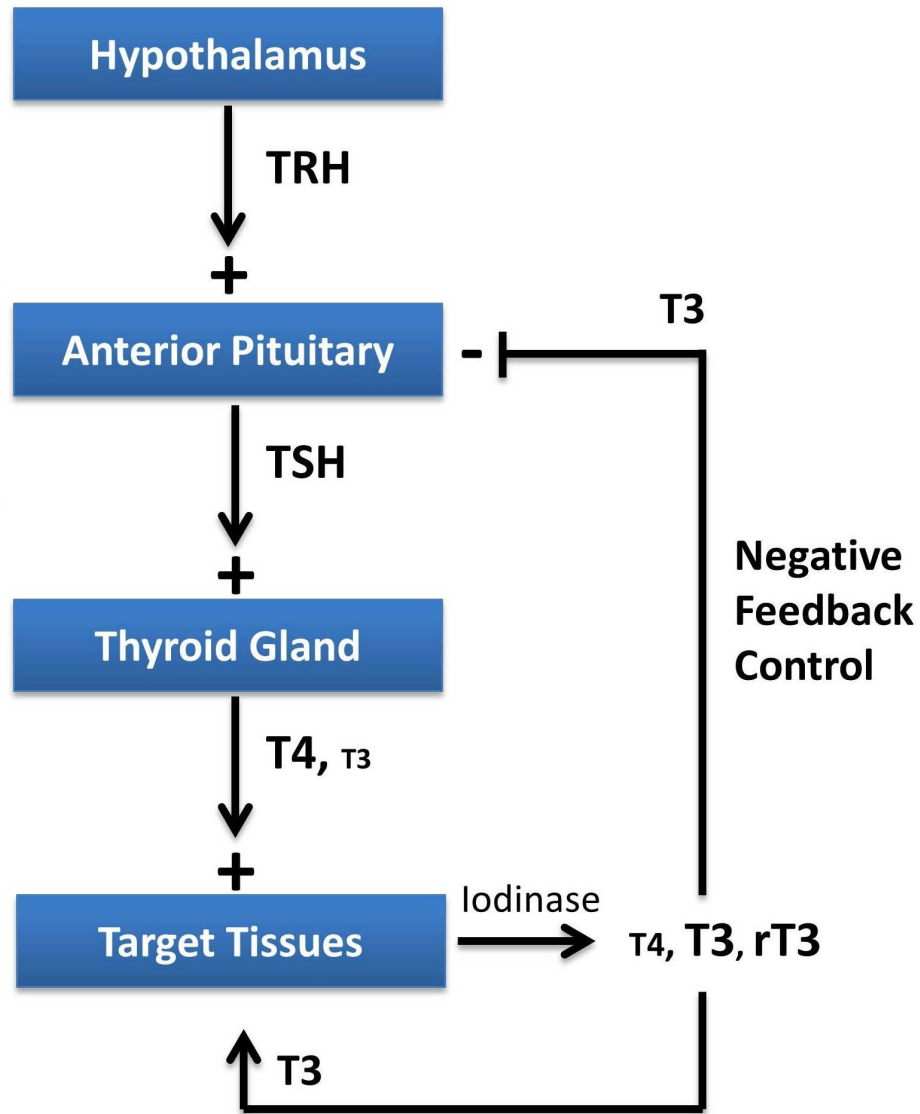




Hyperthyroidism (Thyrotoxicosis)



Thyroid gland



- Thyroid gland secretes T4 and to a lesser extent T3
- Thyroid hormone production is regulated by TSH secreted by the anterior pituitary, which in turn is under negative feedback control by the circulating level of free thyroid hormone and the positive influence of hypothalamic TRH.
- *Thyroid disorders* involve thyroid hormone production or secretion and result in alterations in metabolic stability.

• Pathophysiology

- Tissues are exposed to excessive levels of T4, T3, or both.
- Hyperthyroidism, which is one cause of thyrotoxicosis, refers to the overproduction of thyroid hormone by the thyroid gland.
- TSH-secreting pituitary tumors occur sporadically & they are unresponsive to normal feedback control.
- The tumors may cosecrete prolactin or growth hormone; therefore, patients may present with amenorrhea, galactorrhea, or signs of acromegaly.

- **Graves' disease** is the **most common** cause of hyperthyroidism, which results from the action of **TSAb** directed toward the **thyrotropin receptor** on the surface of thyroid cells.
- An autonomous thyroid nodule (**toxic adenoma**) is **a benign** thyroid mass that produces thyroid hormone **independent** of pituitary TSH control.
- In **multinodular goiter**, follicles with autonomous function coexist with normal or even nonfunctioning follicles.
- **Painful subacute** (granulomatous or de Quervain) **thyroiditis** often develops **after a viral syndrome**.
- **Painless** (silent, lymphocytic, or postpartum) **thyroiditis** is a common cause of thyrotoxicosis. Its etiology may be attributed to **autoimmunity**

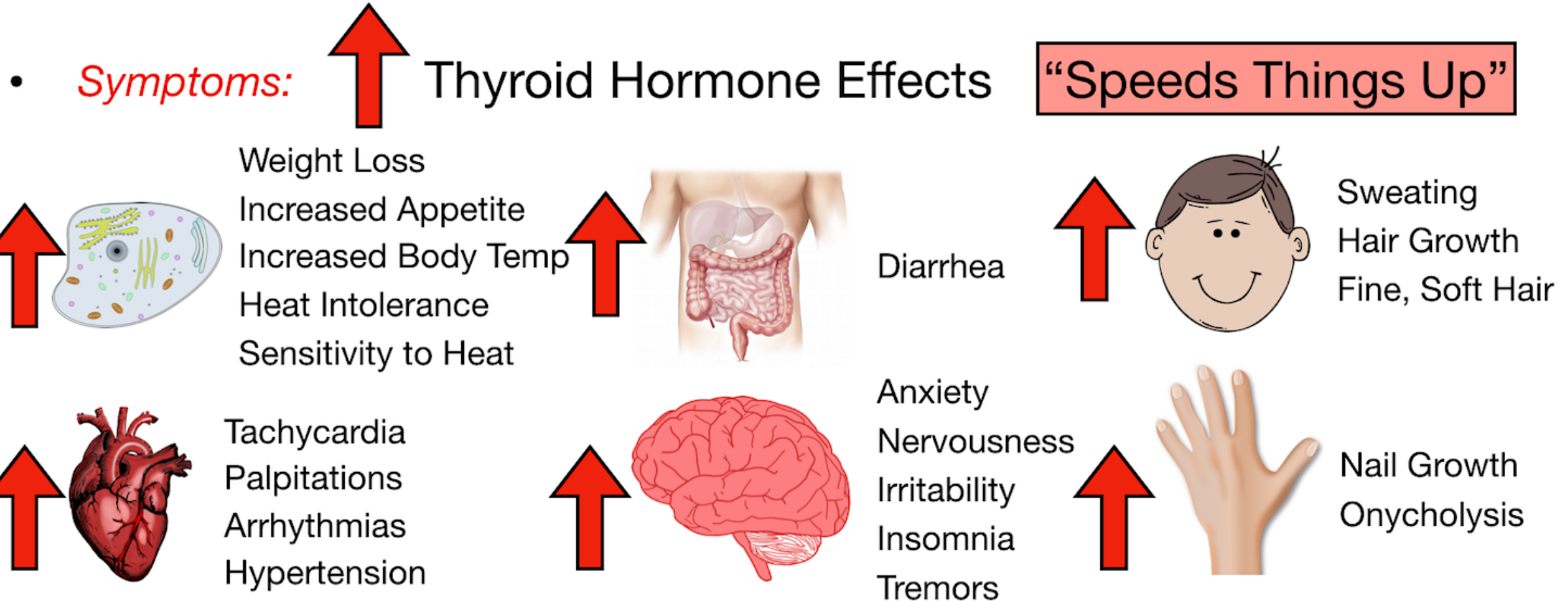
- **Thyrotoxicosis factitia** is hyperthyroidism due to **ingestion** of **exogenous** thyroid hormone.
- **Amiodarone** may induce **thyrotoxicosis** (2%–3% of patients), overt **hypothyroidism** (5% of patients), **subclinical hypothyroidism** (25% of patients), or **euthyroid hyperthyroxinemia**.

- **Clinical presentation**

- **Symptoms** include **nervousness**, anxiety, **palpitations**, easy fatigability, **heat intolerance**, **weight loss concurrent with increased appetite**, increased frequency of bowel movements, and **scanty** or irregular **menses** in women.
- **Physical signs** include warm, smooth, moist skin, and unusually fine hair; onycholysis; **tachycardia at rest**, systolic ejection murmur; occasional gynecomastia in men; **fine tremor** of the protruded tongue and outstretched hands
- **Thyromegaly** is usually present.

Hyperthyroidism Symptoms

Increased Levels of Thyroid Hormone in the Blood



Healthy



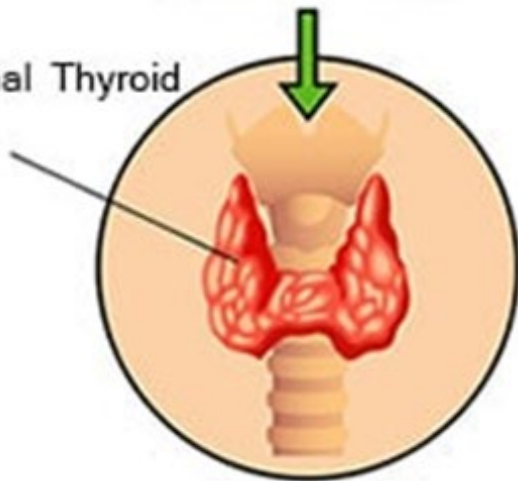
Hyperthyroidism



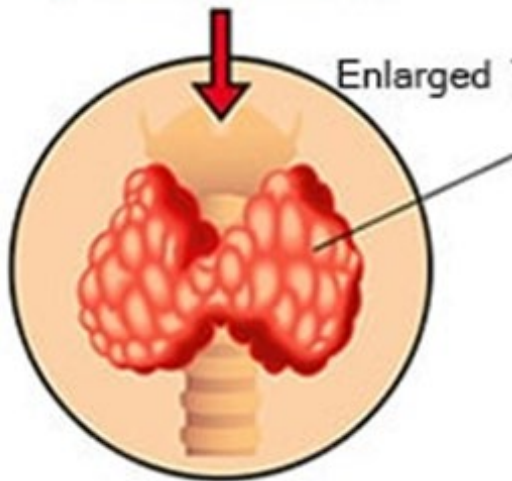
Bulging Eyes

Goiter

Normal Thyroid



Enlarged Thyroid



- **Graves' disease**
- is manifested by **hyperthyroidism, diffuse thyroid enlargement, and extrathyroidal findings of exophthalmos, and pretibial myxedema.**

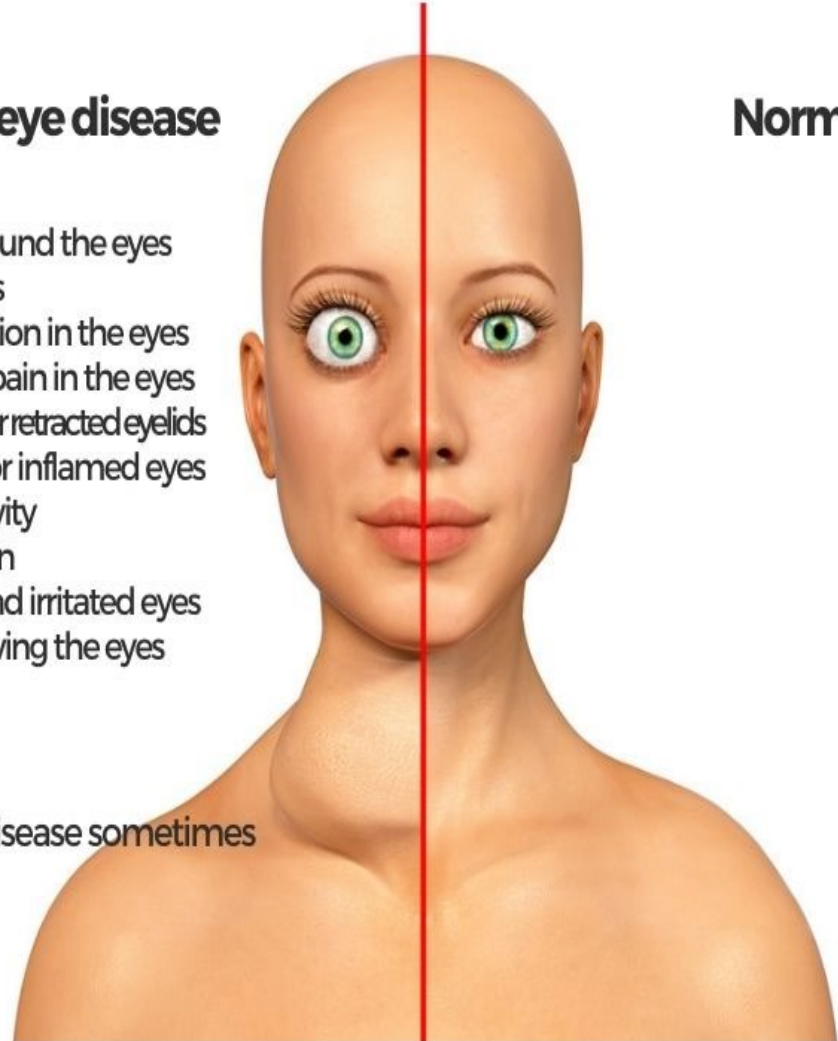
GRAVES' EYE DISEASE SYMPTOMS

GRAVES' OPHTHALMOPATHY OR GRAVES' ORBITOPATHY (GO)

Graves' eye disease

Normal

- Swelling around the eyes
 - Bulging eyes
 - Gritty sensation in the eyes
 - Pressure or pain in the eyes
 - Puffy eyelids or retracted eyelids
 - Reddened or inflamed eyes
 - Light sensitivity
 - Double vision
 - Dry, gritty, and irritated eyes
 - Trouble moving the eyes
 - Vision loss
-
- In graves disease sometimes also goiter



Pretibial myxedema.



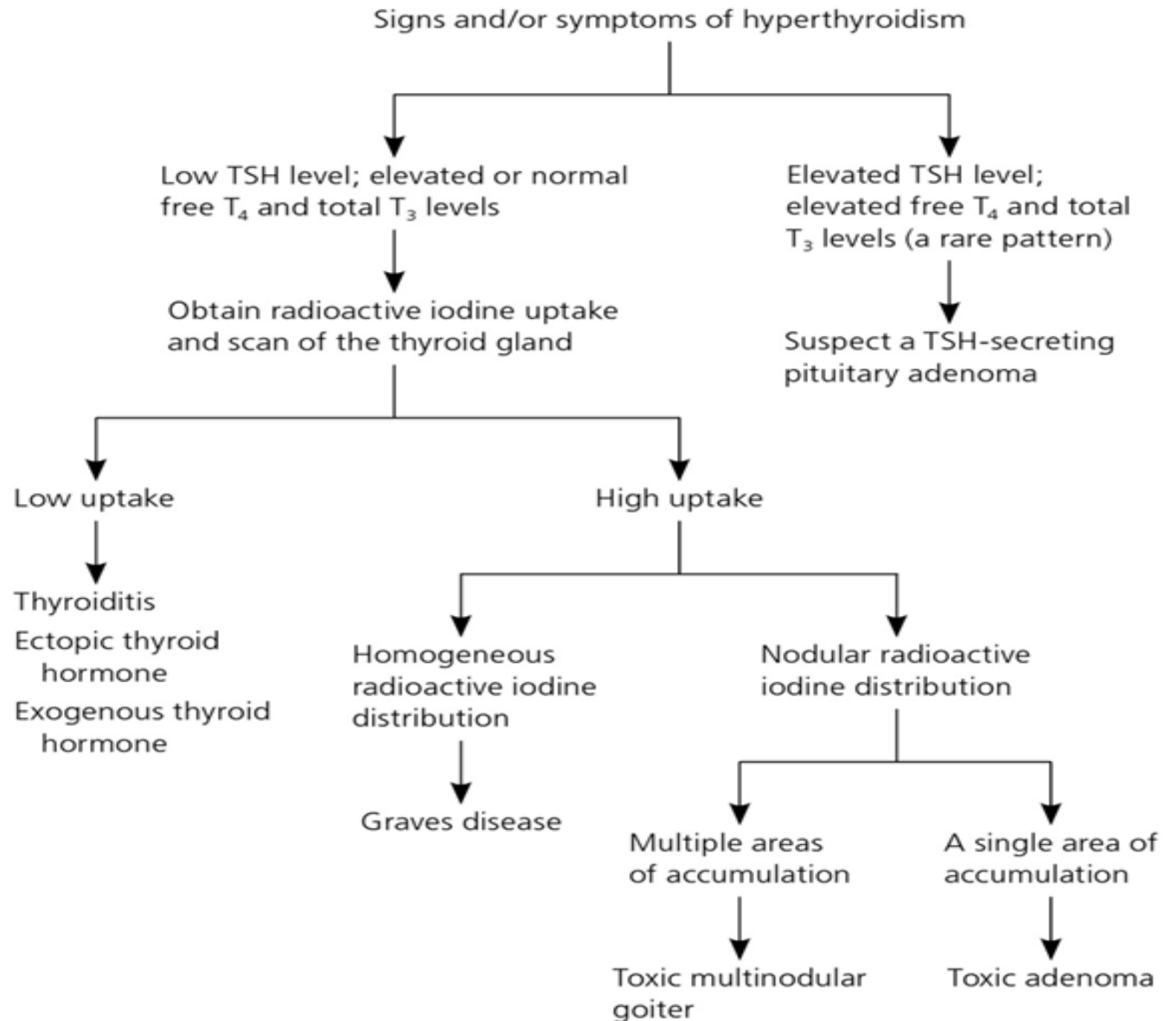
Exophthalmos



Thyroid storm

- Thyroid storm is a life-threatening medical emergency characterized by decompensated thyrotoxicosis, high fever (often $>39.4^{\circ}\text{C}$), tachycardia, tachypnea, vomiting, diarrhea, dehydration, delirium, and coma.
- Precipitating factors of thyroid storm: infection, trauma, surgery, radioactive iodine (RAI) treatment, and withdrawal from antithyroid drugs.

Diagnosis



• **Diagnosis**

- **Elevated 24-hour RAI uptake** indicates **true** hyperthyroidism: The patient's thyroid gland is overproducing T4, T3, or both (normal RAIU 10%–30%).
- A **low RAIU** indicates that excess thyroid hormone is likely caused by **thyroiditis**, **follicular cancer**, or **exogenous** thyroid hormone ingestion.
- In thyrotoxic **Graves' disease**, there is an increase in the overall hormone production rate with a **disproportionate** increase in T3 relative to T4

- In **multinodular goiters**, a thyroid scan shows patchy areas of autonomously functioning thyroid tissue.
- **TSH** levels become **undetectable** in **primary** disorders
- **TSH-induced** hyperthyroidism (**secondary**) is diagnosed by evidence of peripheral hypermetabolism, diffuse thyroid enlargement, **elevated free (T3 and T4)** levels, and **elevated serum TSH** concentrations.
- Because the **pituitary gland** is **extremely sensitive** to even minimal elevations of free T4, a “**normal**” or elevated TSH level in any thyrotoxic patient indicates inappropriate production of TSH.

- In **subacute thyroiditis**, thyroid function tests typically run a **triphasic** course in this self-limited disease.
- **Initially**, serum T4 levels are elevated
- As the disease **progresses**, intrathyroidal hormone stores are depleted, and the patient may become mildly hypothyroid
- During the **recovery phase**, thyroid hormone stores are replenished, and serum TSH elevation gradually normalize.
- Thyrotoxicosis **factitia** should be suspected in a **thyrotoxic** patient **without evidence** of increased hormone production, thyroidal inflammation, or ectopic thyroid tissue + **low RAIU**

• Treatment

• Non-Pharmacologic therapy

- **Surgical removal** of the thyroid gland is considered in patients with a **large gland** (>80 g), **severe ophthalmopathy**, or **lack of remission** on antithyroid drug treatment.
- If thyroidectomy is planned, **methimazole** is given until the patient is **biochemically euthyroid** (usually **6–8 weeks**), followed by addition of **iodides** (500 mg/day) for **10–14 days** before surgery to decrease vascularity of the gland.
- **Propranolol** has been used for **several weeks preoperatively** and **7–10 days postoperatively** to maintain **pulse rate <90 beats/min.**

- **Pharmacologic therapy**

- **A- Thionamides**

- **Methimazole** and **PTU** block thyroid hormone synthesis by inhibiting the **peroxidase** enzyme. **PTU** (but not methimazole) also inhibits **peripheral conversion** of T4 to T3.
- Usual initial doses of **methimazole** can be given in **two or three** divided doses and **PTU** in **three or four** divided doses.
- Evidence exists that both drugs can be given as a single daily dose.

- **Improvement** in symptoms & laboratory abnormalities should occur within **4–8 weeks**, at which time a tapering regimen to maintenance doses can be started.
- Make **monthly dosage changes** because the endogenously produced T4 will reach a new steady state in this interval.
- Continue therapy for **12–24 months** to induce **long-term remission**.
- Monitor patients **every 6–12 months after remission**. If a **relapse** occurs, **alternate** therapy with **RAI** is preferred over a second course of antithyroid drugs, because subsequent courses are less likely to induce remission.

- **Major A/E**: **agranulocytosis** (with fever, malaise, gingivitis, oropharyngeal infection, and granulocyte count $<250/\text{mm}^3$), **aplastic anemia**, **lupus-like syndrome**, **hepatotoxicity**, and **hypoprothrombinemia**.
- If **agranulocytosis** occurs, it usually develops in the **first 3 months** of therapy; routine WBC count monitoring is **not** recommended because of its **sudden onset**.
- Because of the risk of **serious hepatotoxicity**, **PTU** should **not** be considered **first-line** therapy in either adults or children.
- **Exceptions** to this recommendation: (1) the first trimester of pregnancy (when the risk of methimazole-induced embryopathy may exceed that of PTU-induced hepatotoxicity), (2) intolerance to methimazole, and (3) thyroid storm.

• 2- Iodides

- **Acutely blocks** thyroid hormone release, inhibits biosynthesis, & **decreases** size and vascularity of the gland.
- **Symptom improvement** occurs **within 2–7 days** of initiating therapy, and serum T4 and T3 concentrations may be reduced for a few weeks.
- Iodides are often used as **adjunctive** therapy to **prepare** a patient with Graves' disease **for surgery**, to **acutely** inhibit thyroid hormone release & **quickly** attain euthyroid state in severely thyrotoxic patients with cardiac decompensation, or to inhibit thyroid hormone release after RAI therapy.

- Potassium iodide is available as a **saturated solution** (SSKI, 38 mg iodide per drop) or as **Lugol solution**.
- When used to prepare a patient for surgery, it should be administered 7–14 days preoperatively.
- As an **adjunct to RAI**, **SSKI** should not be used before but rather **3–7 days after RAI** so that RAI can concentrate in the thyroid.
- **A/E:** hypersensitivity reactions (skin rashes, rhinitis, conjunctivitis),
- Salivary gland swelling, **“iodism”** (metallic taste, burning mouth and throat, sore teeth and gums, and sometimes stomach upset and diarrhea), and gynecomastia.
- Iodide is **contraindicated** in **toxic multinodular goiter** because the autonomous tissue utilizes the iodine for subsequent thyroid hormone synthesis.

• **3- Beta-adrenergic blockers**

- Used to **ameliorate symptoms** such as palpitations, anxiety, tremor, and heat intolerance.
- They have **no effect** on peripheral thyrotoxicosis and protein metabolism and do not reduce TSAb or prevent thyroid storm.
- β -Blockers are usually used as **adjunctive therapy** with antithyroid drugs, RAI, or iodides when treating Graves' disease or toxic nodules, in **preparation for surgery**, or in **thyroid storm**.
- The **only conditions** for which β -blockers are **primary** therapy for thyrotoxicosis are those **associated with thyroiditis**.

- Propranolol orally four times daily is effective for most patients (heart rate <90 beats/min).
- β -Blockers are contraindicated in decompensated heart failure unless it is caused solely by tachycardia (high output).
- Side effects include nausea, vomiting, anxiety, insomnia, lightheadedness, bradycardia, and hematologic disturbances.
- Centrally acting sympatholytics (eg, clonidine) and calcium channel antagonists (eg, diltiazem) may be useful for symptom control when contraindications to β -blockade exist.

• 4- Radioactive iodine

- Sodium iodide–131 is an oral liquid that concentrates in the thyroid and initially disrupts hormone synthesis by incorporating into thyroid hormones and thyroglobulin.
- Over a period of weeks, follicles that have taken up RAI and surrounding follicles develop cellular necrosis.
- RAI is the agent of choice for Graves' disease, toxic autonomous nodules, and toxic multinodular goiters.
- Pregnancy is an absolute contraindication to use of RAI
- β -Blockers are the primary adjunctive therapy to RAI because they may be given anytime without compromising RAI therapy.

- If **iodides** are administered, they should be given **3–7 days after RAI** to **prevent interference with uptake** of RAI in the thyroid gland.
- Administering **antithyroid** drug therapy **immediately after RAI** may result in a higher rate of posttreatment **recurrence** or **persistent hyperthyroidism**.
- Patients with **cardiac disease and elderly** patients are often treated with **thionamides prior to RAI** ablation because thyroid hormone levels transiently increase after RAI treatment due to **release of preformed** thyroid hormone.

- Use of **lithium as adjunctive** therapy to RAI has **benefits** of increased cure rate, shortened time to cure, and prevention of posttherapy increases in thyroid hormone levels.
- A **single dose** of 4000–8000 rad results in a euthyroid state in **60%** of patients at **6 months or sooner**.
- A **second dose** of RAI should be given **6 months after** the first RAI treatment if the patient remains hyperthyroid.
- **Hypothyroidism commonly** occurs months to years after RAI.
- **Long-term** follow-up has **not** revealed an increased risk for development of mutations or congenital defects.

• **Treatment of thyroid storm**

- Initiate the following **promptly**: (1) suppression of thyroid hormone formation and secretion, (2) antiadrenergic therapy, (3) administration of corticosteroids, and (4) treatment of precipitating factors.
- **PTU** in **large doses** may be the **preferred** thionamide because it blocks peripheral conversion of T4 to T3 in addition to interfering with thyroid hormone production.
- **Iodides**, which rapidly block the release of preformed thyroid hormone, should be **administered after a thionamide** is initiated **to inhibit iodide utilization by the overactive** gland.

- **Antiadrenergic** therapy with the short-acting agent **esmolol** is preferred because it can be used in patients with pulmonary disease or at risk for cardiac failure and because its effects can be rapidly reversed.
- **Corticosteroids** are generally recommended; their benefits may be attributed to their **antipyretic** action and **stabilization of BP**.
- **General supportive measures**, including acetaminophen as an antipyretic (**avoid aspirin or other NSAIDs**, which may displace bound thyroid hormone), fluid and electrolyte replacement, sedatives, digoxin, antiarrhythmics, insulin, and antibiotics should be given as indicated.

• **Evaluation of therapeutic outcomes**

- Evaluate patients **monthly** until they reach a euthyroid condition.
- Assess for clinical signs of continuing thyrotoxicosis or development of hypothyroidism.
- If T4 replacement is initiated, the goal is to maintain both the free T4 level and the TSH concentration in the normal range.
- **Once a stable dose** of T4 is identified, monitor the patient **every 6–12 months**.



•The End