

Hypothyroidism

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• Pathophysiology

- The vast majority of patients have primary hypothyroidism due to thyroid gland failure caused by chronic autoimmune thyroiditis (Hashimoto disease).
- B lymphocytes produce thyroid antibodies.

- **Iatrogenic hypothyroidism occur with:**

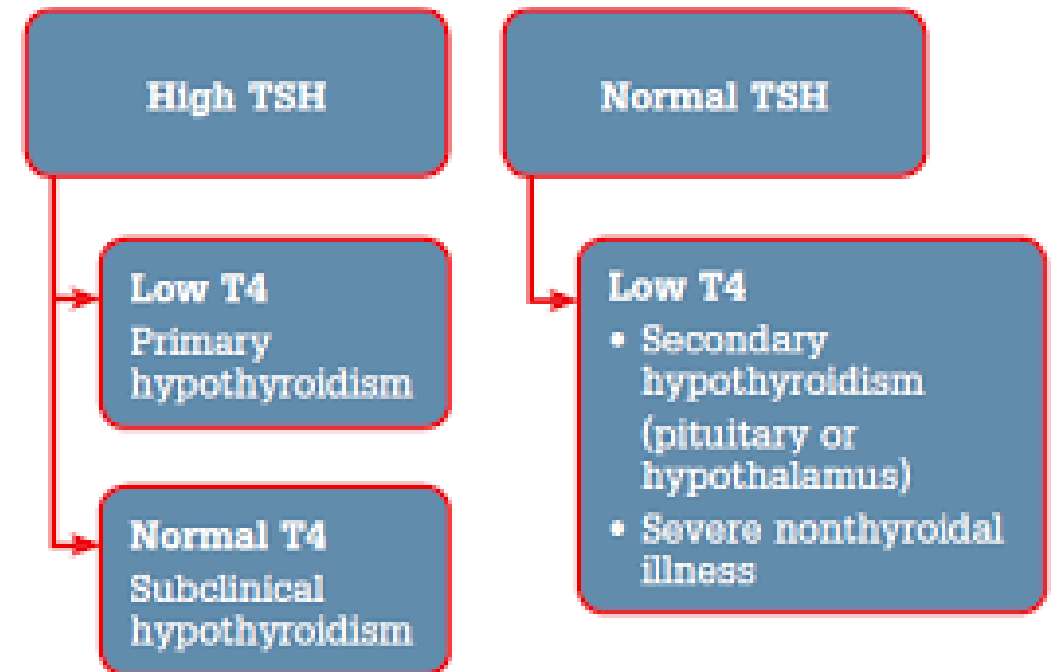
- exposure to destructive amounts of **radiation**,

- after **total thyroidectomy**, or

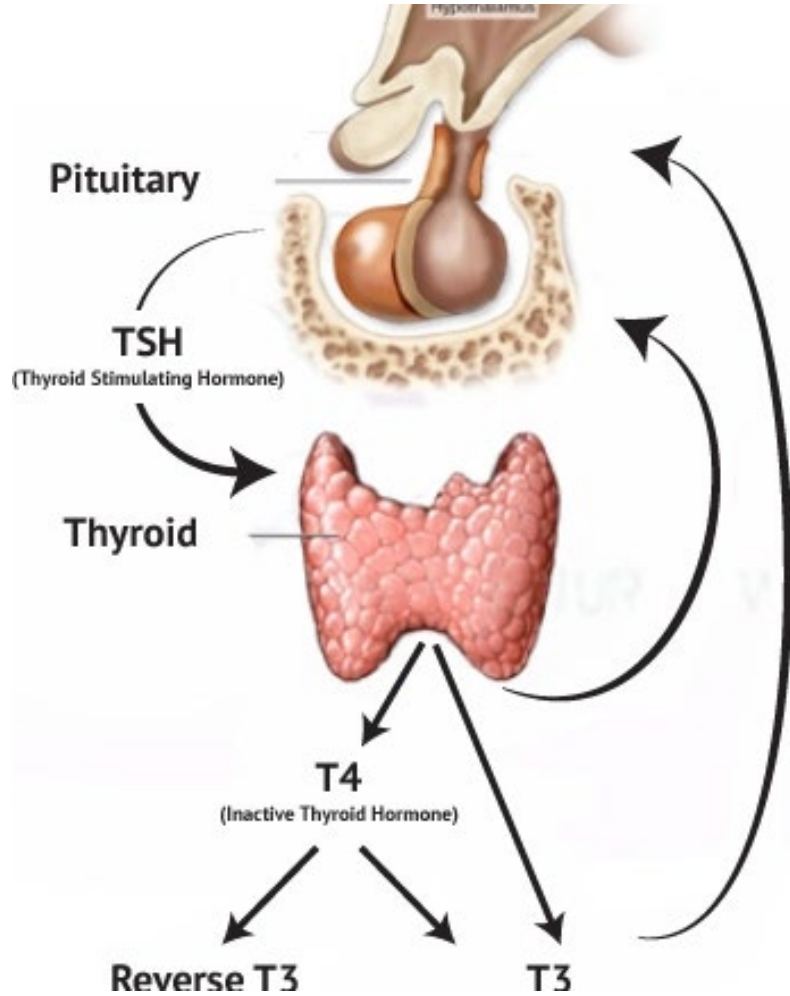
- with **excessive thionamide** doses used to treat hyperthyroidism.

- **Other causes of primary hypothyroidism include iodine deficiency and thyroid hypoplasia.**

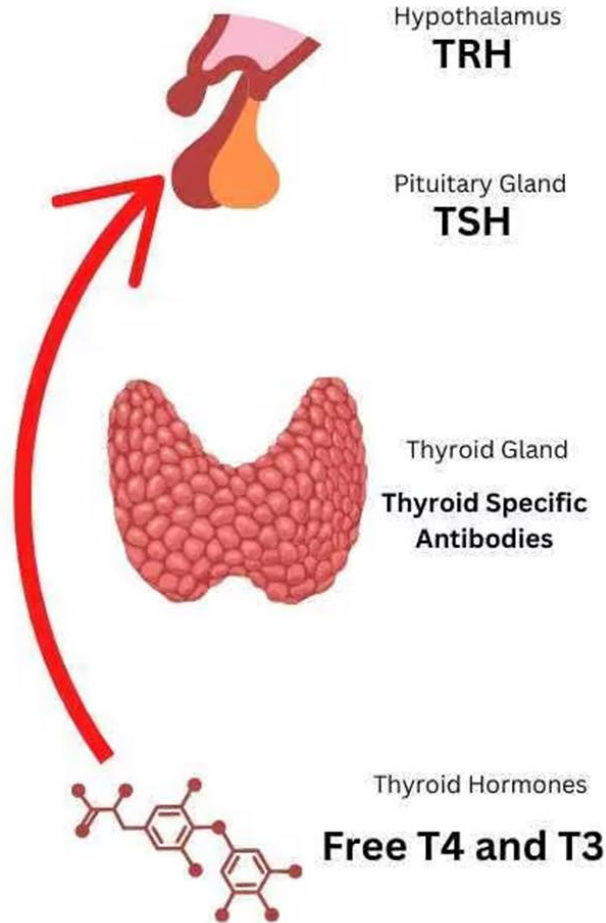
- **Secondary** hypothyroidism due to pituitary failure is **uncommon**.
- Pituitary insufficiency may be caused by destruction of thyrotrophs by pituitary tumors, surgical therapy, external pituitary radiation, or **postpartum pituitary necrosis (Sheehan syndrome)**



Secondary hypothyroidism



Negative feedback inhibition of TRH and TSH secretion by active thyroid hormone (Free T3)



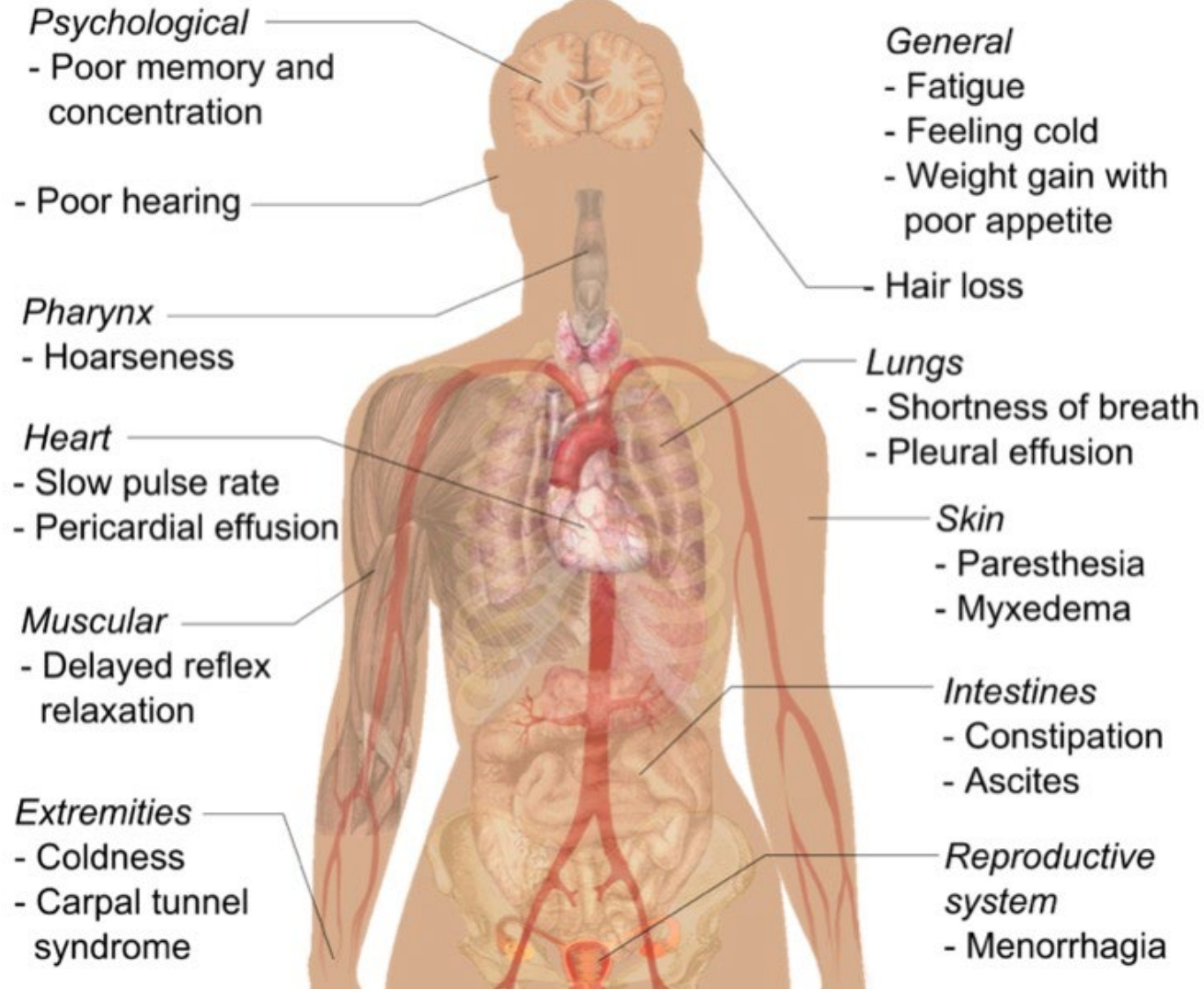
Primary Hypothyroidism	Secondary Hypothyroidism
↑	↓
↑	↓
+	-
↓	↓

• Clinical presentation

- **Symptoms:** dry skin, cold intolerance, weight gain despite anorexia, constipation, lethargy, depression, fatigue, loss of ambition or energy, and myalgia. Menorrhagia and infertility are common in women.
- In children, growth or intellectual retardation.
- Physical signs include coarse skin and hair, cold or dry skin, periorbital puffiness, bradycardia, and hoarse speech.



Signs and symptoms of Hypothyroidism

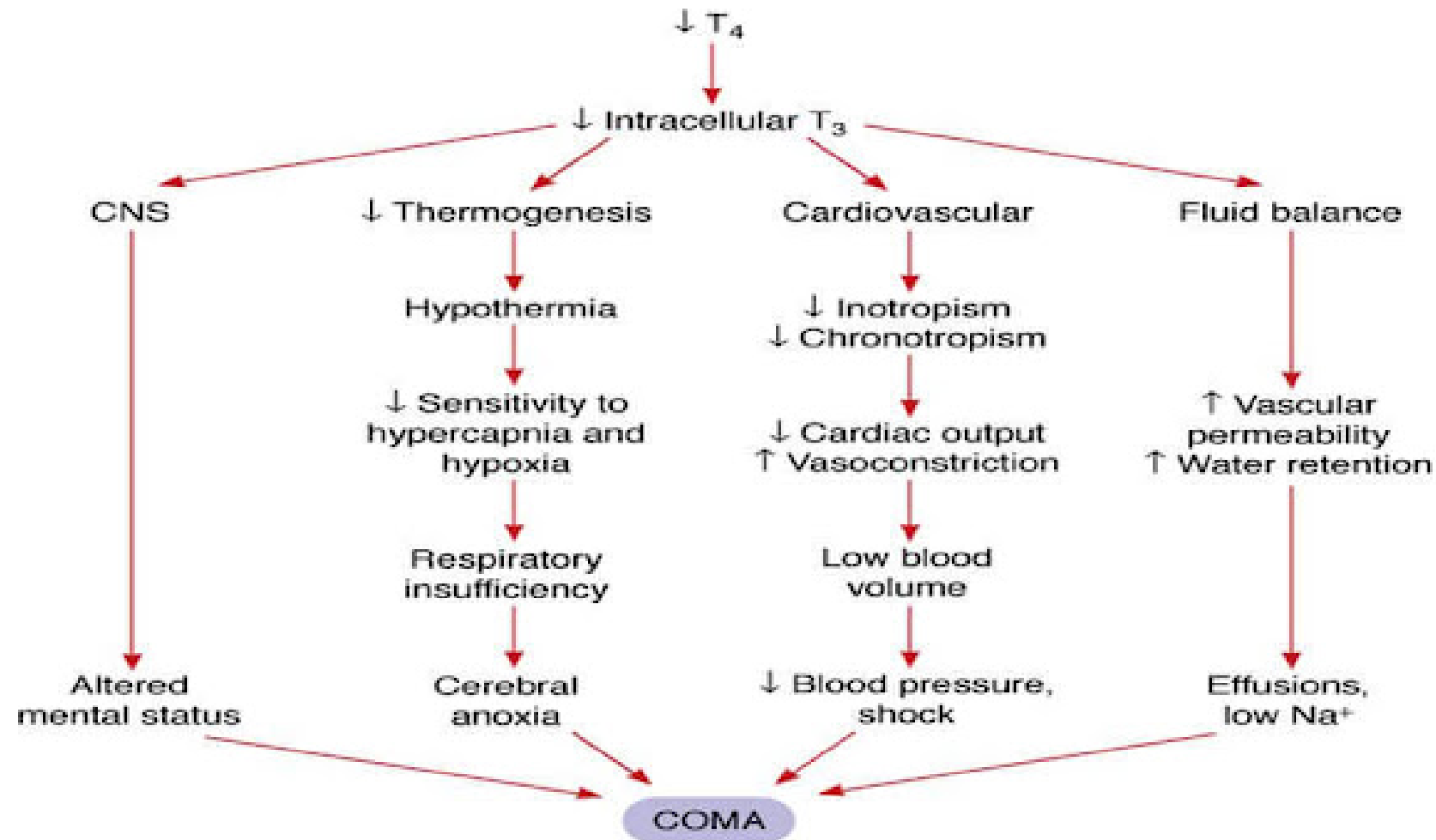


- Patients with **secondary** hypothyroidism due to inadequate TSH production have signs of **generalized pituitary insufficiency**, such as abnormal menses and decreased libido, or evidence of a **pituitary adenoma**, such as visual field defects.

Myxedema coma

- **Myxedema coma** is a rare consequence of **decompensated** hypothyroidism manifested by **hypothermia**, **advanced** stages of hypothyroid symptoms, and **altered sensorium** ranging from **delirium to coma**.
- **Mortality rates** of 60%–70% necessitate immediate and aggressive therapy.

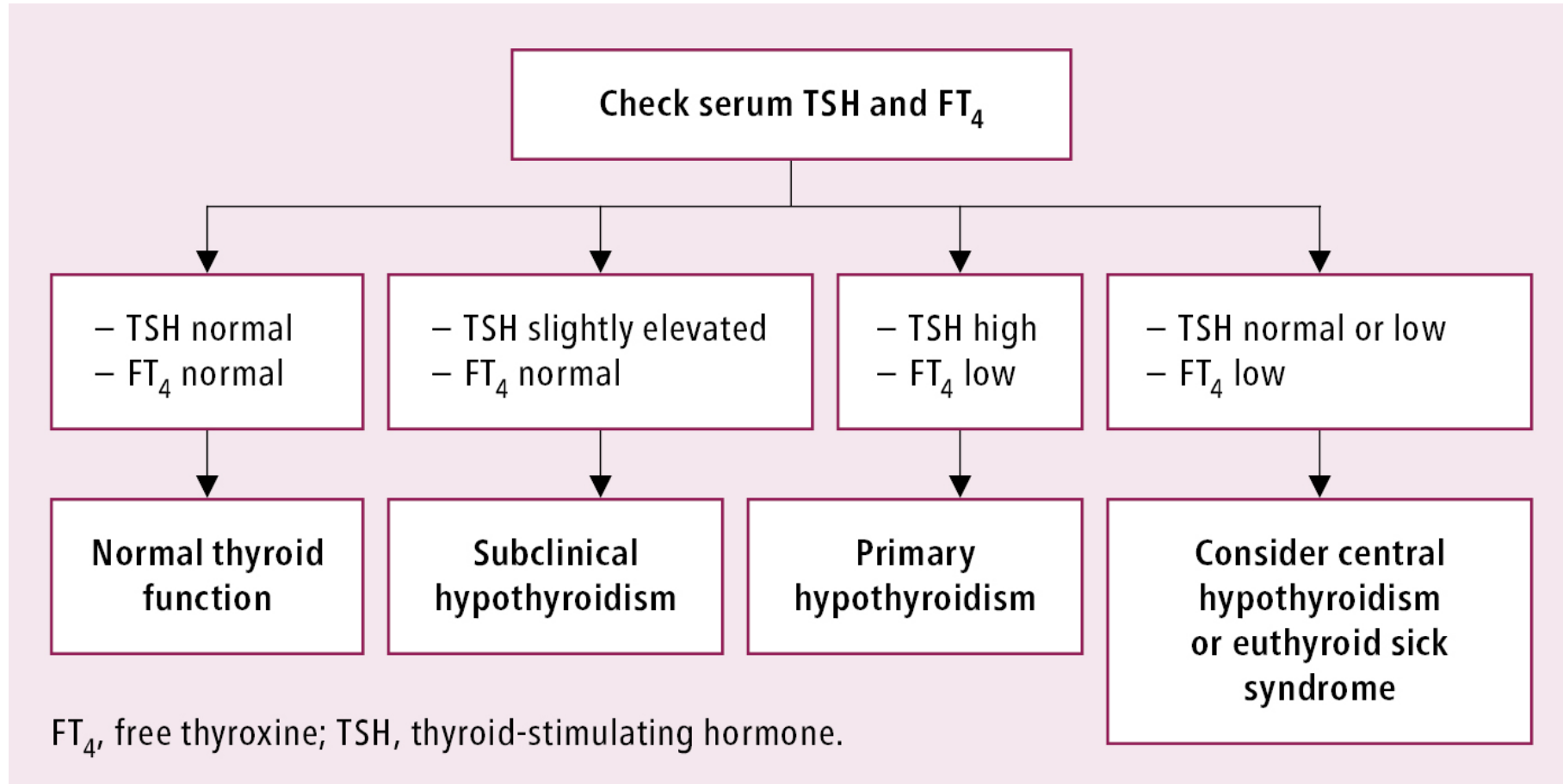
Pathogenesis of myxedema coma



• **Diagnosis**

- A rise in TSH level is the first evidence of primary hypothyroidism.
- Many patients initially have a free T4 level within the normal range (compensated or subclinical hypothyroidism) and few, if any, symptoms of hypothyroidism.
- The T3 concentration is often maintained in the normal range despite low T4.
- In secondary hypothyroidism: serum TSH is generally low or normal. A serum TSH in the normal range is inappropriate if the patient's T4 is low.

Diagnosis



Diagnostic tests

For patients suspected of having hypothyroidism, serum thyroid function (including thyroid-stimulating hormone [TSH], triiodothyronine [T3], and thyroxine [T4]) and thyroid antibody tests are performed.

Test	Normal range
TSH	0.4 – 4.0 mU/L
T4	0.6 – 1.6 ng/dL
T3	230 – 619 pg/dL
Thyroid antibody test	Negative
Results	Diagnosis
↓T3/T4, ↑TSH	Primary hypothyroidism
↓T3/T4, ↓TSH	Secondary hypothyroidism
Positive antibody	Hashimoto's disease

Source: Lewandowski 2015

•Treatment

•Goals:

- Restore thyroid hormone concentrations in tissue,
- provide symptomatic relief,
- prevent neurologic deficits in newborns and children,
- and reverse the biochemical abnormalities of hypothyroidism.

- **Levothyroxine** (L-thyroxine) is the **drug of choice** for thyroid hormone replacement therapy **because** it is chemically stable, relatively inexpensive, active when given orally, free of antigenicity, and has uniform potency.
- Because **T3** is the **biologically active** form, L-thyroxine administration results in a pool of thyroid hormone that is readily and consistently converted to T3.



- In patients with longstanding disease and older individuals without known cardiac disease, start therapy with levothyroxine 50 mcg daily and **increase after 1 month**.
- The recommended initial dose for **older patients** with known **cardiac disease** is 25 mcg/day titrated upward in increments of 25 mcg at monthly intervals to **prevent stress on the CVS**.
- The average maintenance dose for most adults is **~125 mcg/day**, but there is **a wide range** of replacement doses, necessitating **individualized therapy** and appropriate **TSH monitoring** to determine an appropriate dose.

- L-thyroxine is the drug of choice for **pregnant women**.
- **Liothyronine** (synthetic **T3**) has uniform potency but has a **higher incidence** of cardiac adverse effects, higher cost, and difficulty in monitoring with conventional lab tests.
- It must be administered **three times** a day and may require a prolonged adjustment period to achieve stable euthyroidism.
- **Liotrix** (synthetic T4:T3 in a 4:1 ratio) is chemically stable, pure, and has a predictable potency but is **expensive**. It also **lacks therapeutic rationale** because most T3 is converted peripherally from T4.

- **Drug interaction:**
- **Acid suppression** with histamine blockers and PPIs may **reduce** levothyroxine absorption.
- **Drugs that increase nondeiodinative T4 clearance** include rifampin, carbamazepine, and possibly phenytoin.
- **Selenium deficiency and amiodarone may block conversion of T4 to T3**

Adverse effects:

- Excessive doses of thyroid hormone may lead to heart failure, angina pectoris, and MI.
- Hyperthyroidism leads to reduced bone density and increased risk of fracture.

- **Treatment of myxedema coma**

- **Immediate** and aggressive therapy with **IV bolus**

- levothyroxine. with IV hydrocortisone**

- Initial treatment with **IV liothyronine** or a combination of both hormones has also been advocated because of impaired conversion of T4 to T3.

- Give glucocorticoid with **IV hydrocortisone** **until coexisting** adrenal suppression is **ruled out**.

- **Consciousness, lowered TSH concentrations, and improvement in vital signs are expected within 24 hours.**
- **Maintenance levothyroxine doses are typically 75–100 mcg IV until the patient stabilizes and oral therapy is begun.**
- **Provide supportive therapy to maintain adequate ventilation, euglycemia, BP, and body temperature.**
- **Diagnose and treat underlying disorders such as sepsis and MI.**

- **Treatment of Myxedema Coma (table 216-5)**
- Recognition
- Supportive therapy including ventilatory support
- Thyroid replacement
 - Liothyronine 300-500 mcg slow IVP followed by 50-100 mcg daily or
 - T3 25 mcg IV or PO q 8 hrs
- Glucocorticoid
 - Hydrocortisone: 100 mg IV q8h
- Hypothermia
 - Prevent additional loss
 - Passive external rewarming
- Electrolyte correction
 - Gentle fluid restriction for dilutional hyponatremia
 - Hypertonic saline for severe hyponatremia
- Hypoglycemia
 - Dextrose-containing IV fluids
 - Monitoring
- Aggressive treatment of precipitating causes
- Admit patient to a monitored setting

• **Evaluation of therapeutic outcomes**

- Serum **TSH level** is the **most** sensitive and specific monitoring parameter **for adjustment** of levothyroxine dose.
- Concentrations are usually **normalized** within **2–6 weeks**.
- **Check both** TSH and T4 concentrations **every 6 weeks** until a euthyroid state is achieved.
- An elevated TSH level indicates insufficient replacement.
- **Serum T4** concentrations can be useful in **detecting** noncompliance, malabsorption, or **changes in levothyroxine product bioequivalence**.

- In patients with hypothyroidism caused by hypothalamic or pituitary failure, alleviation of the clinical syndrome and restoration of serum T4 to the normal range are the only criteria available for estimating the appropriate replacement dose of levothyroxine.



•The End