

به نام خداوند جان و خرد

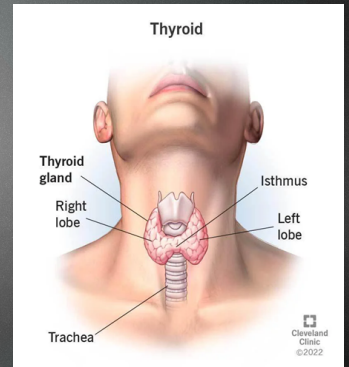
بیماری کم کاری تیروئید

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مدیر برنامه کشوری غربالگری نوزادان

دی 1402 28



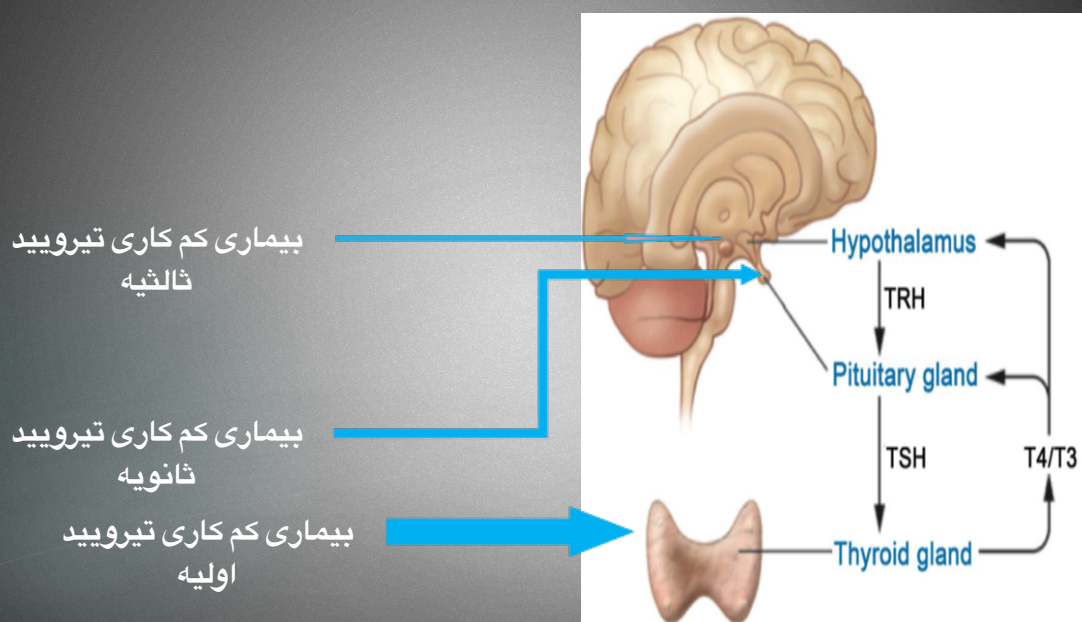
مباحث مورد بحث

- تعریف و انواع کم کاری تیروئید
 - اتیولوژی
 - علایم و نشانه‌ها
 - تشخیص
 - مدیریت
- تشخیص افتراقی
- عوارض

مقدمه

- هورمون تیروئید برای تکامل طبیعی و تنظیم متابولیسم کلیه سلول های و ارگان های بدن ضروری است.
- تیروکسین ترشح می شود 100-125 nmol روزانه
- نیمه عمر تیروکسین 7-10 روز است.
- کم کاری تیروئید:
 - وضعیت بالینی شایعی است که به علت کمبود هورمون تیروئید به وجود می آید و در صورت عدم تشخیص و درمان مناسب، منجر به اثرات نامطلوب سلامتی بر بسیاری از ارگان های بدن، بخصوص سیستم قلبی- عروقی می شود.
 - در همه سنین بروز می کند.
 - علل و تظاهرات متعددی دارد.
 - و کمبود ید از شایع ترین علل کم کاری تیروئید هستند Hashimoto thyroiditis

انواع بیماری کم کاری تیروئید بر اساس آناتومی



Common Causes of Primary Hypothyroidism

Etiology	Mechanism/pathophysiology
Chronic autoimmune thyroiditis (Hashimoto thyroiditis)	Failure of T cell-mediated inflammatory response, cytokine release, infiltration of the thyroid by lymphocytes and development of fibrotic tissue in the thyroid
Disturbed iodine metabolism	- Iodine deficiency leads to decreased thyroid hormone production - Iodine excess leads to thyroid hypofunction in patients with underlying primary thyroid disease
Irradiation and/or thyroidectomy	Ablation of thyroid cells
Genetic disease	Loss of function, pathogenetic variants
Infiltrative diseases and lymphoma	Infiltration of various cells or materials, granuloma and fibrosis formation, and thyroid cell destruction
Infection and/or inflammation	Thyroid cell destruction (most recently COVID-19 infection)
Medications	- Lithium: increased intr-athyroid iodine content, decreased coupling of iodotyrosine and hormone release - IFNα / Type 1 interferon (and IL-2 (Interleukine-2): possible activation of autoimmune process - Tyrosine kinase inhibitors: multiple mechanisms described, including effects on thyroid hormone metabolism and transport, and destructive thyroiditis - Immune-checkpoint inhibitors: immune-related adverse events, including immune-mediated thyroiditis, autoimmune subacute thyroiditis

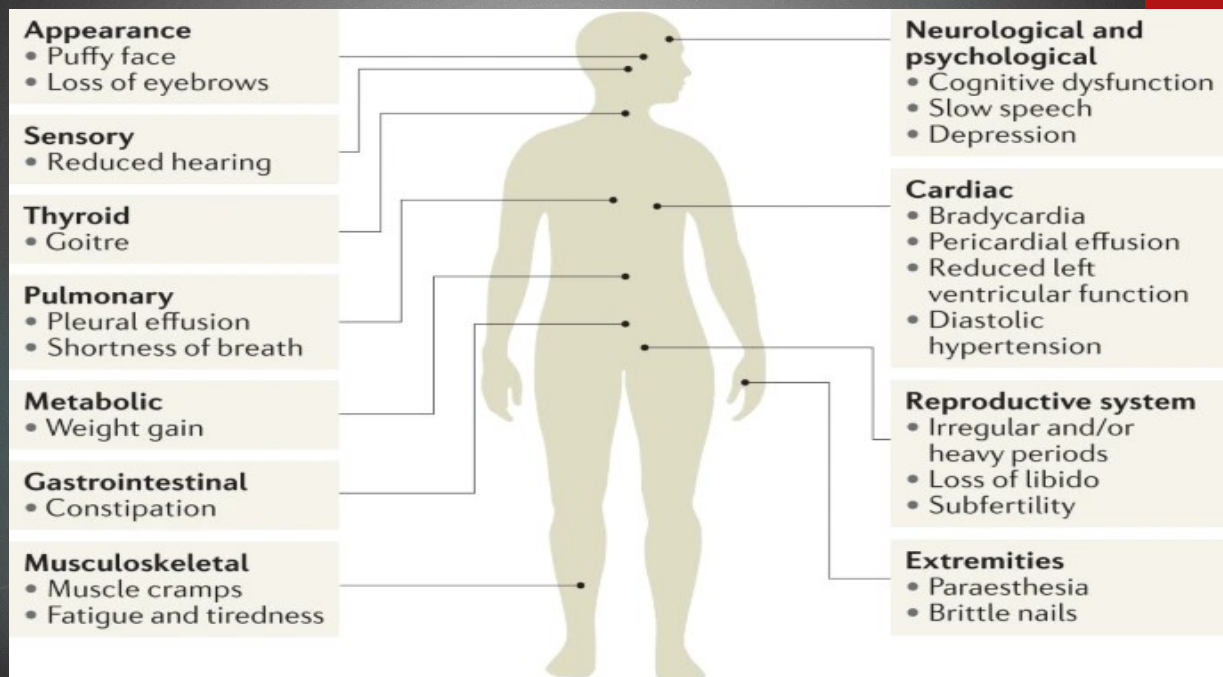
Common Causes of Central hypothyroidism (*Hypothalamic or Pituitary*)

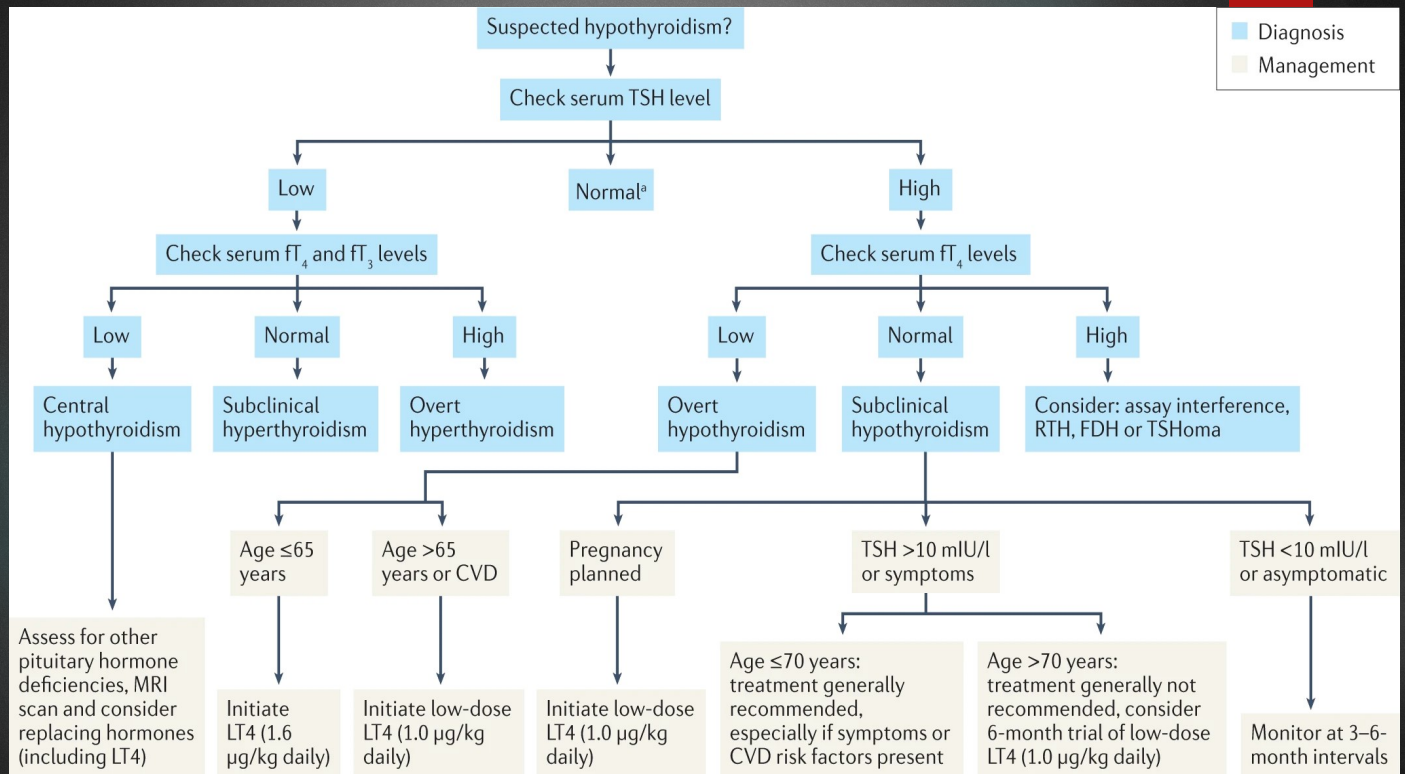
Etiology	Mechanism/pathophysiology
Pituitary or hypothalamic lesions and/or damage	Heterogeneous mechanisms leading to altered secretion of TSH by thyrotrophs and/or bioactivity of TSH, involving both hypothalamic and pituitary structures, usually combined with other pituitary hormone deficiencies, including surgery, head trauma, neoplastic lesions, apoplexy, pituitary necrosis, (partial) empty sella, infiltrative lesions or irradiations
Infection and/or inflammation	Infectious (for example, tuberculosis) or inflammatory (for example, sarcoidosis) causes leading to pituitary or hypothalamic infiltration or hypophysitis (for example, due to immune-checkpoint inhibitors)
Congenital	Midline defects, Rathke pouch cyst or genetic mutation; congenital genetic mutations rarely cause isolated central hypothyroidism but are more often part of combined pituitary hormone deficiencies and the most common defective genes are PROP1 and POU1F1

Common Causes of Peripheral hypothyroidism (peripheral tissues)

Etiology	Mechanism/pathophysiology
Consumptive hypothyroidism	Increased expression of type 3 iodothyronine deiodinase (for example, by tumor cells)
Resistance to thyroid hormone	Tissue-specific hypothyroidism owing to decreased sensitivity to thyroid hormone (resulting from mutations in, for example, MCT8, THRA or THRB)

Common symptoms and signs associated with hypothyroidism





Management

• Treatment can:

- leads to resolution of hypothyroidism symptoms in most patients
- reduce tissue manifestations
- improve quality of life and might also benefit neurodevelopment in infants and young children.

• Thyroid hormone replacement with LT_4

• Full replacement doses in adults are **1.6 $\mu g/kg/day$**

• Central hypothyroidism:

- TSH levels are largely uninformative
- serum FT_4 level in the upper half of the reference range

• Serum TSH levels should be monitored **6 weeks after initiation** of treatment or any change in dose and then **every 6–12 months** thereafter

• LT_4 should be taken consistently, **30-60 min on an empty stomach**

Management ...

- **Individuals >65–70 years of age** are at increased risk of adverse effects from excessive LT4 dosing, including:
 - Cardiac arrhythmia, Progressive heart failure, increased bone turnover leading to Osteoporosis, Catabolic muscle loss, impaired Quality of life and increased Mortality.
- It is often recommended to start with low LT4 doses (**25–50 µg daily**) and to titrate doses gradually, particularly in those with known cardiovascular disease.
- It is also important to avoid overtreatment and targeting a serum TSH levels of **4–6 mIU/l** has been advocated in patients **>70 years of age**.

Management ...

• In pregnant:

- The developing fetus relies entirely on maternal thyroid hormones during critical phases of early brain development (usually before gestation weeks 16–20).
- Untreated overt hypothyroidism in pregnancy is associated with increased risks for **miscarriage, preterm delivery, gestational hypertension, pre-eclampsia, low birthweight, fetal death and impaired child intellectual development**.
- Serum TSH levels should be closely monitored, approximately **every 4 weeks during the first half of gestation**.
- In pregnancy and the pre-conception period, LT4 dosing should target a serum TSH level of **<2.5 mIU/l**.
- Hypothyroidism following postpartum thyroiditis is common and may be transient.

Medications that alter thyroid hormone absorption

Medications	Mechanism	Effect on LT4 requirements
Calcium carbonate, Calcium citrate or calcium acetate; Ferrous sulfate; Proton-pump inhibitors; Aluminium hydroxide; Sucralfate; Raloxifene; Bile acid sequestrants	Decreased LT4 absorption	Increased (if LT4 not taken 4 h apart)
Phenytoin; Phenobarbital; Carbamazepine; Rifampin; Tyrosine kinase inhibitors	Increased thyroid hormone metabolism	Increased
Bile acid sequestrants	Reduced enterohepatic thyroid hormone circulation	Increased
Oral oestrogens; Selective oestrogen receptor modulators; Mitotane; Opiates; 5-fluorouracil	Increased TBG	Increased
Androgens; Nicotinic acid; Chronic glucocorticoid therapy; Danazol; L-asparaginase	Decreased TBG	Decreased
Amiodarone	Inhibition of 5'-deiodination (inhibits production of T3 from T4)	Increased

LT4 = levothyroxine; T3 = triiodothyronine; T4 = thyroxine; TBG = thyroxine-binding globulin

Sub-clinical Hypothyroidism

Subclinical hypothyroidism (SCH) is characterized by elevated TSH and normal free T4

Summary of Key Contents in Clinical Guidelines for Managing Subclinical Hypothyroidism

Guidelines	Consideration of LT4 treatment
ATA (2012)	TSH >10 mIU/L, age <70 years TSH 4–10 mIU/L, age <65 years, symptoms (+)
ETA (2013)	TSH >10 mIU/L, age <70 years TSH <10 mIU/L, age <70 years, symptoms (+) TSH <10 mIU/L, age >70 years, symptoms (+) or high cardiovascular (CV) risk
Clinical practice guideline (2017)	TSH >10 mIU/L, age <70 years, symptoms (+) or CV risk factors (6 months of LT4 treatment in the cases of TSH >4.5 and <7 mIU/L with symptoms or TSH >7 and <10 mIU/L, age <70 years symptoms (+) regardless of age, CV risk factors, TPOAb)
NICE guideline (2018)	TSH >10 mIU/L, age <70 years TSH 4–10 mIU/L, age <65 years, symptoms (+)
Clinical practice guideline (2019)	Only women who are or trying to become pregnant Patients with TSH >20 mIU/L
KTA (2023)	TSH >10 mIU/L, age <70 years

Management ...

- **Refractory Hypothyroidism** the use of supra-therapeutic doses of LT4(is the failure to control hypothyroidism despite LT4 doses of 1.9 µg/kg/day or higher.
- **Causes:**
 - Poor treatment adherence
 - Gastrointestinal Disorders
- **Complications:**
 - Bone
 - Heart

Differential diagnoses of hypothyroidism

Endocrine conditions

- **Addison disease:** may present with increased thyroid-stimulating hormone levels that normalize after glucocorticoid replacement is commenced
- **Obesity** (particularly if associated with obstructive sleep apnoea)
- **Menopause**
- **Hypopituitarism**
- **Type 1 diabetes mellitus**
- **Hypercalcaemia**

Autoimmune conditions

- **Coeliac Disease**
- **Pernicious Anemia**
- **Rheumatoid Arthritis**

Differential diagnoses of hypothyroidism ...

Chronic End Organ Damage Conditions

- Chronic Kidney Disease
- Chronic Liver Disease
- Chronic Heart Failure

Hematological conditions

- Anemia
- Multiple Myeloma

Nutritional deficiencies

- Vitamin B1, B12 or D deficiency
- Folate Deficiency

Differential diagnoses of hypothyroidism ...

Mental Health Conditions

- Depression
- Anxiety
- Chronic Stress
- Poor Sleep Pattern

Myxoedema Coma:

- Myxoedema coma is the most extreme form of hypothyroidism and can progress to death unless diagnosed and treated promptly.
- It has a **mortality rate of 50–60%**.
- It is more commonly seen in **older women** in **winter** and might present with the typical signs of **severe hypothyroidism** as well as **hypothermia**, **hyponatraemia**, **hypercarbia** and **hypoxaemia**.
- It is critical that treatment with **thyroid hormone therapy** is initiated promptly, ideally in an intensive care unit (ICU) setting.
- The type of thyroid hormone to administer (T4, T3 or both) is unclear.
- In addition, to thyroid hormone therapy, adjunctive measures, such as ventilation, warming, fluids, antibiotics, vasopressor agents and corticosteroids, are equally essential for survival.

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- 3) Juan Eduardo Quiroz-Aldave , Marcio José Concepción-Zavaleta , María del Carmen Durand-Vásquez , Luis Alberto Concepción-Urteaga , Elman Rolando Gamarra-Osorio , et al. Refractory Hypothyroidism: Unraveling the Complexities of Diagnosis and Management. Endocrine Practice. Volume 29, Issue 12, 2023, Pages 1007-1016.
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پیروز باشید