

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ**  
**Харківський національний медичний університет**

**DISEASES OF ENDOCRINE SYSTEM  
HYPOTHYREOSIS. CLASSIFICATION,  
DIAGNOSIS, CLINICAL PRESENTATION,  
TREATMENT. THYROIDITIS**

*Methodological recommendations  
for students of IV course*

**ЗАХВОРЮВАННЯ ЕНДОКРИННОЇ СИСТЕМИ.  
ГІПОТИРЕОЗ. КЛАСИФІКАЦІЯ, ДІАГНОСТИКА,  
КЛІНІКА, ЛІКУВАННЯ. ТИРЕОЇДИТ**

*Методичні вказівки  
для студентів IV курсу*

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**MODULE 1 «THE FUNDAMENTALS OF DIAGNOSIS, TREATMENT  
AND PREVENTION OF MAIN DISEASES OF THE ENDOCRINE SYSTEM»  
TOPIC «HYPOTHYREOSIS. CLASSIFICATION, DIAGNOSIS, CLINICAL  
PRESENTATION, TREATMENT. THYROIDITIS»**

**The purpose:**

1. To determine the etiologic and pathogenic factors of hypothyroidism (HT) and thyroiditis (T).
2. To acquaint students with classifications of HT and T
3. Determination of typical clinical presentation of HT.
4. To acquaint students with the clinical variants of T.
5. To acquaint students with possible complications of HT.
6. To determine the basic diagnostic criteria of HT.
7. To determine the basic diagnostic criteria of T.
8. To draft the plan of examination of patient with HT.
9. To draft the plan of examination of patient with T.
10. To analyze the results of laboratory and instrumental studies for diagnosis of HT.
11. To analyze the results of laboratory and instrumental studies for diagnosis of T.
12. To perform differential diagnosis of HT.
13. To perform differential diagnosis of acute T.
14. To perform differential diagnosis of chronic T.
15. Substantiation and formulation of diagnosis of HT.
16. To draft the plan of treatment of patients with HT and T.
17. Deontological and psychological peculiarities of management of HT patients.

**What a student should know?**

1. Determination of HT, T.
2. Epidemiology of HT and T in the world.
3. Risk factors for HT and T.
4. The mechanism of hormonal and metabolic disorders in HT and T.
5. Etiology and pathogenesis of HT and T.
6. Clinical presentation of HT and T.
7. Typical clinical presentation of HT.
8. Multiple organ complications of HT.
9. Diagnostic criteria for HT and T.
10. The indications for use and analysis of results of hormonal assays.
11. The diagnostic value of ultrasonography of thyroid gland, radioisotope study of thyroid gland (radiometry, scanning).
12. The choice of method of treatment of HT and T.

**What a student should be able to do?**

1. To define the risk factors for HT and T.
2. To diagnose HT and T.
3. To perform palpation of thyroid gland.
4. To determine the degree of thyroid gland enlargement.
5. To diagnose the syndrome of HT.
6. To determine the severity of HT.
7. To define the character of multiple organ complications of HT.
8. To analyze the results of hormonal assays and functional tests.
9. To evaluate the results of ultrasonography and radioisotope study of thyroid gland.
10. To perform differential diagnostics of HT syndrome.
11. To evaluate the dynamics of thyroid status of patients against the background of use of thyroid preparations.
12. To be able to correct the dose of thyroid preparations as well as side preparations depending on achievement of the euthyroid state by the patients.
13. To draft a long-term plan of HT prevention and treatment of its complications, including the seasonal correction of replacement therapy doses.
14. Cooperation with allied specialists (surgeon, ophthalmologist, cardiologist, neurologist) on the stage of making of complete diagnosis and prolonged supervision of patient with HT or T.

**Content of topic:**

Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone.

Hypothyroidism occurs at any age but is particularly common among the elderly. It occurs in close to 10 % of women and 6 % of men > 65. Although typically easy to diagnose in younger adults, it may be subtle and manifest atypically in the elderly.

**Primary hypothyroidism:**

Primary hypothyroidism is the most common one (95 % of patients) and develops due to disease in the thyroid; thyroid-stimulating hormone (TSH) is increased. The most common cause is autoimmune. It usually results from Hashimoto's thyroiditis and is often associated with a firm goiter or, later in the disease process, with a shrunken fibrotic thyroid with little or no function. The second most common cause is post-therapeutic hypothyroidism, especially after radioactive iodine therapy or surgery for hyperthyroidism or goiter. Hypothyroidism during overtreatment with propylthiouracil, methimazole, and iodide abates after therapy is stopped.

Most patients with non-Hashimoto's goiters are euthyroid or have hyperthyroidism, but goitrous hypothyroidism may occur in endemic goiter. Iodine deficiency decreases thyroid hormonogenesis. In response, TSH is released, which causes the thyroid to enlarge and trap iodine avidly; thus, goiter results. If iodine deficiency is severe, the patient becomes hypothyroid, a rare occurrence in the majority of developed countries since the advent of iodized salt.

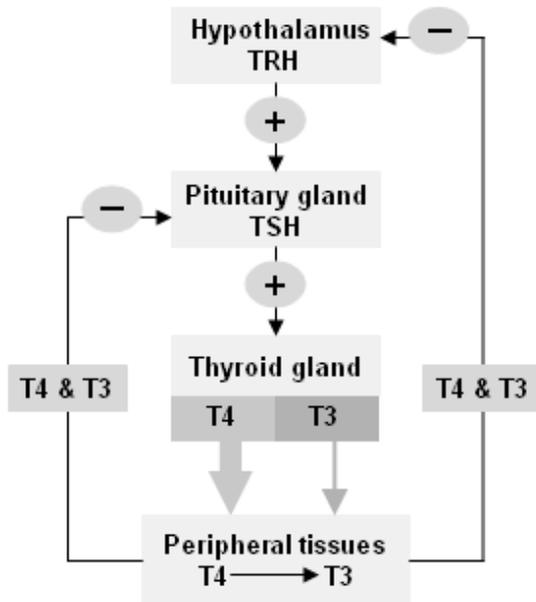
Iodine deficiency can cause congenital hypothyroidism. In severely iodine-deficient regions worldwide, congenital hypothyroidism (previously termed endemic cretinism) is a major cause of intellectual disability.

Rare inherited enzymatic defects can alter the synthesis of thyroid hormone and cause goitrous hypothyroidism.

Hypothyroidism may occur in patients taking lithium, perhaps because lithium inhibits hormone release by the thyroid. Hypothyroidism may also occur in patients taking amiodarone or other iodine-containing drugs, and in patients taking interferon alfa. Hypothyroidism can result from radiation therapy for cancer of the larynx or Hodgkin lymphoma. The incidence of permanent hypothyroidism after radiation therapy is high, and thyroid function (through measurement of serum TSH) should be evaluated at 6- to 12-months intervals.

**Secondary hypothyroidism:**

Secondary hypothyroidism occurs when the hypothalamus produces insufficient thyrotropin-releasing hormone (TRH) or the pituitary produces insufficient TSH. Sometimes, deficient TSH secretion due to deficient TRH secretion is termed tertiary hypothyroidism.



**Figure 1.** The hypothalamic-pituitary-thyroid axis. Levels of circulating thyroid hormones are regulated by a complex feedback system involving the hypothalamus and pituitary gland

## Pathogenesis

Clinical hypothyroidism indicates a pervasive deficit in thyroid hormone actions, including modulation of calorogenesis (resulting in hypothermia), decreasing oxygen consumption in most tissues and additional organ-specific effects. Disorders of protein metabolism lead to slower protein synthesis and breakdown, derangements of glycosaminoglycans metabolism, accumulation of glycoprotein mucin and hyaluronic acid in tissues. The excess of these substances changes the colloidal structure of connective tissue, increases its hydrophilicity and binds sodium, altogether causing the formation of myxedema. The mechanism of water and sodium accumulation in tissues may also be influenced by the excessive vasopressin, which production is normally inhibited by thyroid hormones. The following description of the basis for thyroid hormone action summarises how deficient triiodothyronine actions at the genomic level cause biochemical, hormonal, ion transport, and mechanical changes in target tissues. Thyroxine, the principal product of the thyroid gland and circulating thyroid hormone, is converted by outer-ring monodeiodination to triiodothyronine in the cytoplasm and nucleus of target tissues by three distinct tissue specific deiodinases. Most classic thyroid hormone actions are believed to be mediated genomically by triiodothyronine binding to one of the triiodothyronine receptor isoforms (TR $\alpha$ 1, TR $\beta$ 1, and TR $\beta$ 2), which are members of the nuclear receptor superfamily. Triiodothyronine receptors possess domains for triiodothyronine binding, DNA binding, and coupling with another triiodothyronine receptor or other nuclear receptor (eg, retinoic acid X receptor) to form dimers. The receptors bind to DNA at sites with certain specific orientations of paired thyroid response elements with specific hexameric oligonucleotide sequences that are typically located in the 5' regulatory regions of thyroid hormone-responsive genes. In most cases, interaction of triiodothyronine with its receptor prompts the binding of accessory protein cofactors that either activate or repress a specific gene's transcription (as triiodothyronine does to the hypothalamic thyroid releasing hormone and thyrotrophic thyrotropin  $\beta$  subunit genes).

Based on this model, some clinical manifestations of hypothyroidism are understood at the molecular level. For example, failure to stimulate the growth hormone gene in pituitary somatotrophs causes short stature in prepubertal children; a deficit in expression of the hepatic LDL receptor gene mediated by thyroid hormone regulated SREBP2 (sterol regulatory element binding transcription factor 2) decreases the rate of LDL-cholesterol clearance, causing hypercholesterolaemia; and decreased expression of myocardial sarcoplasmic reticulum ATPase and  $\alpha$ -myosin heavy chain impairs diastolic and systolic ventricular performance, respectively. Many other clinical manifestations of hypothyroidism are not yet linked to specific genomic actions.

## Symptoms and Signs

Symptoms and signs of primary hypothyroidism are often subtle and insidious. Symptoms may include cold intolerance, constipation, forgetfulness, and personality changes. Modest weight gain is largely the result of fluid retention and decreased metabolism. Paresthesias of the hands and feet are common, often due to carpal-tarsal tunnel syndrome caused by deposition of proteinaceous ground substance in the ligaments around the wrist and ankle. Women with hypothyroidism may develop menorrhagia or secondary amenorrhea.

The facial expression is dull; the voice is hoarse and speech is slow; facial puffiness and periorbital swelling occur due to infiltration with the mucopolysaccharides hyaluronic acid and chondroitin sulfate; eyelids droop because of decreased adrenergic drive; hair is sparse, coarse, and dry; and the skin is coarse, dry, scaly, and thick. The relaxation phase of deep tendon reflexes is slowed. Hypothermia is common. Dementia or frank psychosis (myxedema madness) may occur.

Carotenemia is common, particularly notable on the palms and soles, caused by deposition of carotene in the lipid-rich epidermal layers. Deposition of proteinaceous ground substance in the tongue may cause macroglossia. A decrease in both thyroid hormone and adrenergic stimulation causes bradycardia. The heart may appear to be enlarged on examination and imaging, partly because of dilation but chiefly because of pericardial effusion. Pleural or abdominal effusions also may be noted. The pericardial and pleural effusions develop slowly and only rarely cause respiratory or hemodynamic distress.

Elderly patients have significantly fewer symptoms than do younger adults, and complaints are often subtle and vague. Many elderly patients with hypothyroidism present with nonspecific geriatric syndromes—confusion, anorexia, weight loss, falling, incontinence, and decreased mobility. Musculoskeletal symptoms (especially arthralgias) occur often, but arthritis is rare. Muscular aches and weakness, often mimicking polymyalgia rheumatica or polymyositis, and an elevated CK level may occur. In the elderly, hypothyroidism may mimic dementia or parkinsonism.

Although secondary hypothyroidism is uncommon, its causes often affect other endocrine organs controlled by the hypothalamic-pituitary axis. In a woman with hypothyroidism, indications of secondary hypothyroidism are a history of amenorrhea rather than menorrhagia and some suggestive differences on physical examination. Secondary hypothyroidism is characterized by skin and hair that are dry but not very coarse, skin depigmentation, only minimal macroglossia, atrophic breasts, and low blood pressure. Also, the heart is small, and serous pericardial effusions do not occur. Hypoglycemia is common because of concomitant adrenal insufficiency or growth hormone deficiency.

### **Myxedema coma:**

Myxedema coma is a life-threatening complication of hypothyroidism, usually occurring in patients with a long history of hypothyroidism. Its characteristics include coma with extreme hypothermia (temperature 24° to 32.2 °C), areflexia, seizures, and respiratory depression with CO<sub>2</sub> retention. Severe hypothermia may be missed unless low-reading thermometers are used. Rapid diagnosis based on clinical judgment, history, and physical examination is imperative, because death is likely without rapid treatment. Precipitating factors include illness, infection, trauma, drugs that suppress the CNS, and exposure to cold.

### **Diagnosis**

- TSH
- Free thyroxine (T<sub>4</sub>)

Serum TSH is the most sensitive test, and screening of selected populations is warranted. In primary hypothyroidism, there is no feedback inhibition of the intact pituitary, and serum TSH is always elevated, whereas serum free T<sub>4</sub> is low. In

secondary hypothyroidism, free  $T_4$  and serum TSH are low (sometimes TSH is normal but with decreased bioactivity).

Many patients with primary hypothyroidism have normal circulating levels of triiodothyronine ( $T_3$ ), probably caused by sustained TSH stimulation of the failing thyroid, resulting in preferential synthesis and secretion of biologically active  $T_3$ . Therefore, serum  $T_3$  is not sensitive for hypothyroidism.

Anemia is often present, usually normocytic-normochromic and of unknown etiology, but it may be hypochromic because of menorrhagia and sometimes macrocytic because of associated pernicious anemia or decreased absorption of folate. Anemia is rarely severe (Hb usually  $> 90$  g/L). As the hypometabolic state is corrected, anemia subsides, sometimes requiring 6 to 9 months.

Serum cholesterol is usually high in primary hypothyroidism but less so in secondary hypothyroidism.

### **Treatment:**

*L-Thyroxine, adjusted until TSH levels are in midnormal range*

Various thyroid hormone preparations are available for replacement therapy, including synthetic preparations of  $T_4$  (L-thyroxine),  $T_3$  (liothyronine), combinations of the 2 synthetic hormones, and desiccated animal thyroid extract. L-Thyroxine is preferred; the usual maintenance dose is 75 to 150 mcg per os once/day, depending on age, body mass index, and absorption. The starting dose in young or middle-aged patients who are otherwise healthy can be 100 mcg or 1.7 mcg/kg per os once/day.

However, in the elderly and in patients with heart disease, therapy is begun with low doses, usually 25 mcg once/day. The dose is adjusted every 6 weeks until maintenance dose is achieved. The maintenance dose may need to be decreased in elderly patients and increased in pregnant women. Dose may also need to be increased if drugs that decrease  $T_4$  absorption or increase its biliary excretion are administered concomitantly. The dose used should be the lowest that restores serum TSH levels to the midnormal range (though this criterion cannot be used in patients with secondary hypothyroidism). In secondary hypothyroidism the dose of L-thyroxine should achieve a free  $T_4$  in the midnormal range.

Liothyronine should not be used alone for long-term replacement because of its short half-life and the large peaks in serum  $T_3$  levels it produces. The administration of standard replacement amounts (25 to 37.5 mcg 2/day) results in rapidly increasing serum  $T_3$  to between 300 and 1000 ng/dL (4.62 to 15.4 nmol/L) within 4 hours due to its almost complete absorption; these levels return to normal by 24 hours. Additionally, patients receiving liothyronine are chemically hyperthyroid for at least several hours a day, potentially increasing cardiac risks.

Similar patterns of serum  $T_3$  occur when mixtures of  $T_3$  and  $T_4$  are taken per os, although peak  $T_3$  is lower because less  $T_3$  is given. Replacement regimens with synthetic  $T_4$  preparations reflect a different pattern in serum  $T_3$  response. Increases in serum  $T_3$  occur gradually, and normal levels are maintained when adequate doses of  $T_4$  are given. Desiccated animal thyroid preparations contain variable amounts of  $T_3$  and  $T_4$  and should not be prescribed unless the patient is already taking the preparation and has normal serum TSH.

In patients with secondary hypothyroidism, L-thyroxine should not be given until there is evidence of adequate cortisol secretion (or cortisol therapy is given), because L-thyroxine could precipitate adrenal crisis.

Myxedema coma is treated as follows:

- T<sub>4</sub> given IV;
- Corticosteroids;
- Supportive care as needed;
- Conversion to oral T<sub>4</sub> when patient is stable.

Patients require a large initial dose of T<sub>4</sub> (300 to 500 mcg IV) or T<sub>3</sub> (25 to 50 mcg IV). The IV maintenance dose of T<sub>4</sub> is 75 to 100 mcg once/day and of T<sub>3</sub>, 10 to 20 mcg 2/day until T<sub>4</sub> can be given orally. Corticosteroids are also given because the possibility of central hypothyroidism usually cannot be initially ruled out. The patient should not be rewarmed rapidly, which may precipitate hypotension or arrhythmias. Hypoxemia is common, so PaO<sub>2</sub> should be monitored. If ventilation is compromised, immediate mechanical ventilatory assistance is required. The precipitating factor should be rapidly and appropriately treated and fluid replacement given carefully, because hypothyroid patients do not excrete water appropriately. Finally, all drugs should be given cautiously because they are metabolized more slowly than in healthy people.

### **Subclinical hypothyroidism**

*Subclinical hypothyroidism is elevated serum TSH in patients with absent or minimal symptoms of hypothyroidism and normal serum levels of free T<sub>4</sub>.*

Subclinical thyroid dysfunction is relatively common; it occurs in more than 15 % of elderly women and 10% of elderly men, particularly in those with underlying Hashimoto's thyroiditis.

In patients with serum TSH > 10 mU/L, there is a high likelihood of progression to overt hypothyroidism with low serum levels of free T<sub>4</sub> in the next 10 years. These patients are also more likely to have hypercholesterolemia and atherosclerosis. They should be treated with L-thyroxine, even if they are asymptomatic. For patients with TSH levels between 4,5 and 10 mU/L, a trial of L-thyroxine is reasonable if symptoms of early hypothyroidism like fatigue, depression are present. L-Thyroxine therapy is also indicated in pregnant women and in women who plan to become pregnant to avoid deleterious effects of hypothyroidism on the pregnancy and fetal development. Patients should have annual measurement of serum TSH and free T<sub>4</sub> to assess progress of the condition if untreated or to adjust the L-thyroxine dosage.

## THYROIDITIS, CLASSIFICATION, ETIOLOGY, CLINICAL MOTION, DIAGNOSTICS, TREATMENT

Thyroiditis is a general term that refers to «inflammation of the thyroid gland». Thyroiditis includes a group of individual disorders causing thyroidal inflammation but presenting in different ways.

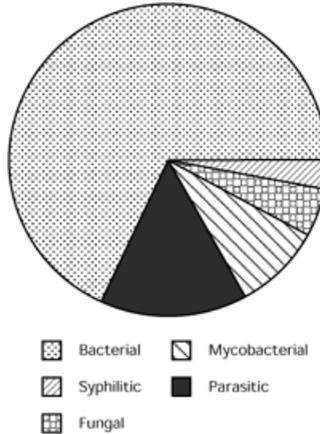
### *Classification:*

1. Acute thyroiditis (diffuse or local):
  - a) suppurative;
  - б) nonsuppurative.
2. Subacute thyroiditis:
  - a) diffuse;
  - б) local.
3. Chronic thyroiditis:
  - a) autoimmune thyroiditis;
  - б) invasive fibrous (Riedel's goiter);
  - в) specific thyroiditis (tuberculous, syphilitic);
  - г) caused by physical or chemical agents;
  - д) parasitic.

### **Acute suppurative thyroiditis**

Acute suppurative thyroiditis, also known as microbial inflammatory thyroiditis, is a rare subtype most often caused by the presence of Gram-positive bacteria in the thyroid gland. *Staphylococcus aureus* is the most common infectious agent, but other organisms have also been implicated (Figure 2). This disorder is rare because of the inherent resistance of the thyroid gland to infection. Microbial inflammatory thyroiditis occurs most often in women 20 to 40 years of age. Most patients have a preexisting thyroid disorder, usually nodular goiter. Anterior neck pain and tenderness are common. Other clinical features include fever, pharyngitis and dermal erythema. The pain is typically worse during swallowing and radiates locally. Tachycardia is common, along with leukocytosis and an elevated ESR (erythrocyte sedimentation rate) level. TSH, T<sub>4</sub> and T<sub>3</sub> levels are typically normal, while RAIU (radioactive iodine uptake) may be normal or show cold nodules in areas of abscess formation. The cause of infection is first determined by culture and sensitivity of samples obtained through fine-needle aspiration.

When the cause of the infection is determined, appropriate parenteral antibiotics should be prescribed. Patients with abscesses require surgical drainage and, possibly, a thyroid lobectomy. Heat, rest and aspirin provide symptomatic relief; steroids may offer additional benefit. The disease is usually self-limited, lasting weeks to months.



**Figure 2.** Causes for acute suppurative thyroiditis

### **Acute nonsuppurative thyroiditis**

The disease develops in a type of aseptic inflammation due to injury and bleeding into the gland, or after radiation therapy. The method of low-dose treatment with radioactive  $I^{131}$  reduced the number of radiation thyroiditis. Before the invention of low-dose method it occurred in about 5 % of cases 2–3 weeks after administration of the radioactive iodine due to destruction of the follicular epithelium.

Patients complain about pain and feeling of pressure in the area of gland, sometimes mild symptoms of thyrotoxicosis: tachycardia, emotional lability, sweating.

Treatment is symptomatic and includes analgesics, beta blockers. Usually disease lasts for 3–4 weeks. Particular attention should be paid to diagnosis of radiation induced thyroiditis in patients with retrosternal location of gland, because the increase of the gland's size due to inflammation can cause compression of the mediastinal organs.

### **Subacute granulomatous thyroiditis (de quervain's thyroiditis)**

Subacute granulomatous thyroiditis, is an acute inflammatory disease of the thyroid caused by a virus.

History of an antecedent viral upper respiratory tract infection is common. Histologic studies show moderate lymphocytic infiltration of the thyroid gland, along with characteristic giant cell infiltration, polymorphonuclear leukocytes, and follicular disruption.

### **Symptoms and Signs**

There is pain in the anterior neck and fever of  $37.8^{\circ}$  to  $38.3^{\circ}$  C. Neck pain characteristically shifts from side to side and may settle in one area, frequently radiating to the jaw and ears. It is often confused with dental pain, pharyngitis, or otitis and is aggravated by swallowing or turning of the head. Symptoms of hyperthyroidism are common early in the disease because of hormone release from the disrupted

follicles. There is more lassitude and prostration than in other thyroid disorders. On physical examination, the thyroid is asymmetrically enlarged, firm, and tender.

### **Diagnosis**

- Clinical findings;
- Free thyroxine (T<sub>4</sub>) and thyroid-stimulating hormone (TSH) levels;
- ESR;
- Radioactive iodine uptake (RAIU).

Diagnosis is primarily clinical, based on finding an enlarged, tender thyroid in patients with the appropriate clinical history. Thyroid testing with TSH and at least a free T<sub>4</sub> measurement is usually also done. Radioactive iodine uptake should be measured to confirm the diagnosis. When the diagnosis is uncertain, fine-needle aspiration biopsy is useful. Thyroid ultrasonography with color Doppler shows reduced blood flow in contrast with the increased flow of Graves' disease. Laboratory findings early in the disease include an increase in free T<sub>4</sub> and triiodothyronine (T<sub>3</sub>), a marked decrease in TSH and thyroid RAIU (often 0), and a high ESR. After several weeks, the thyroid is depleted of T<sub>4</sub> and T<sub>3</sub> stores, and transient hypothyroidism develops accompanied by a decrease in free T<sub>4</sub> and T<sub>3</sub>, a rise in TSH, and recovery of thyroid RAIU. Weakly positive thyroid antibodies may be present. Measurement of free T<sub>4</sub>, T<sub>3</sub>, and TSH at 2- to 4-week intervals identifies the stages of the disease.

### **Prognosis**

Subacute thyroiditis is self-limited, generally subsiding in a few months; occasionally, it recurs and may result in permanent hypothyroidism when follicular destruction is extensive.

### **Treatment**

- NSAIDs
- Sometimes corticosteroids, a  $\beta$ -blocker, or both

Discomfort is treated with high doses of aspirin or NSAIDs. In severe and protracted cases, corticosteroids (prednisone 30 to 40 mg per os once/day, gradually decreasing the dose over 3 to 4 weeks) eradicate all symptoms within 48 hours.

Bothersome hyperthyroid symptoms may be treated with a short course of a  $\beta$ -blocker. If hypothyroidism is pronounced or persists, thyroid hormone replacement therapy may be required, rarely permanently.

## **Chronic autoimmune thyroiditis**

Chronic autoimmune thyroiditis, also known as chronic lymphocytic thyroiditis (Hashimoto's thyroiditis) is the most common inflammatory condition of the thyroid gland and the most common cause of hypothyroidism. It is an autoimmune condition characterized by high titers of circulating antibodies to thyroid peroxidase and thyroglobulin.

### **Epidemiology**

Chronic lymphocytic thyroiditis is the most common cause of hypothyroidism in European countries, and euthyroid persons with Hashimoto's disease develop hypothyroidism at a rate of approximately 5 percent per year. Up to 95 percent of cases of chronic autoimmune thyroiditis occur in women, usually between 30 and 50

years of age. Chronic autoimmune thyroiditis is also the most common cause of sporadic goiter in children.

A genetic predisposition to thyroid auto-immunity exists; it is inherited as a dominant trait. Hashimoto's disease has been linked to other autoimmune diseases, including systemic lupus erythematosus, rheumatoid arthritis, pernicious anemia, diabetes mellitus and Sjögren's syndrome. A rare but serious complication of chronic autoimmune thyroiditis is thyroid lymphoma. These lymphomas, generally the B-cell, non-Hodgkin's type, tend to occur in women 50 to 80 years of age and are usually limited to the thyroid gland.

### **Clinical manifestations and diagnosis**

Although Hashimoto's thyroiditis is usually asymptomatic, some patients may complain of a feeling of tightness or fullness in the neck; however, neck pain and tenderness are rare (Figure 3). At the time of diagnosis, symptoms of hypothyroidism are present in 20 percent of patients. Physical examination generally reveals a firm, irregular, nontender goiter. The ESR and white blood cell count are normal. The definitive indicator of chronic autoimmune thyroiditis is the presence of thyroid-specific autoantibodies in the serum. The three main targets for thyroid antibodies are thyroglobulin (a protein carrier for thyroid hormones), thyroid microsomal antigen (also called thyroid peroxidase) and the thyroid-stimulating hormone (TSH) receptor. Low levels of circulating antibodies are common in other thyroid diseases, such as multinodular goiter and thyroid malignancy. Antithyroid microsomal antibodies in titers greater than 1:6,400 or antithyroid peroxidase antibodies in excess of 200 IU per mL, however, are strongly suggestive of chronic autoimmune thyroiditis. Testing of thyroid autoantibodies and measurement of serum thyroglobulin levels will confirm the diagnosis. RAIU is variable and can be depressed, normal or increased, depending on the extent of follicular destruction. Patchy uptake is common, providing little diagnostically useful information. Ultrasonography shows an enlarged gland with a diffusely hypoechoic pattern in most patients. RAIU and thyroid ultrasonography are not necessary parts of the work-up for this disease. A dominant nodule in a patient with Hashimoto's disease should prompt a fine-needle aspiration biopsy to exclude malignancy.

### **Treatment**

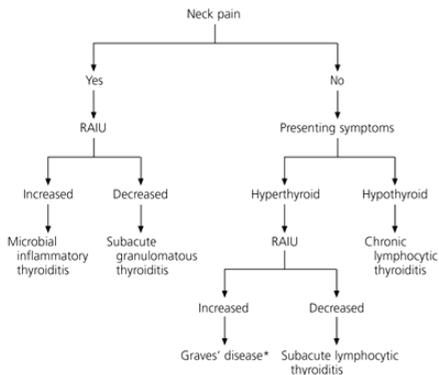
Because thyroiditis is usually asymptomatic and the goiter is small, many patients do not require treatment. When hypothyroidism is present, treatment with thyroxine ( $T_4$ ) is indicated. Thyroid hormone replacement therapy is also indicated in patients with a TSH level in the normal range, to reduce goiter size and prevent progression to overt hypothyroidism in high-risk patients. Lifetime replacement of levothyroxine is indicated in hypothyroid patients, at a starting dosage of 25 to 50 mcg per day, with gradual titration to an average daily dosage of 75 to 150 mcg. A lower starting dosage (12.5 to 25 mcg per day) and a more gradual titration are recommended in elderly patients and in patients with cardiovascular disease. The dosage may be increased in these patients 25 to 50 mcg every four to six weeks until the TSH level is normal.

In patients with an elevated TSH level and a normal thyroxine ( $T_4$ ) level (subclinical hypothyroidism), indications for treatment are less clear. If the TSH level is greater than 20 mU/L with a normal  $T_4$  level, there is a high probability that the

patient will develop hypothyroidism. If the TSH level is elevated but is less than 20 mU/L and the antimicrosomal antibody titer is greater than 1:1,600, hypothyroidism will develop in 80 percent of patients. Therefore, it is recommended that treatment be initiated in patients with symptoms of hypothyroidism, in patients with a serum TSH level greater than 10 mU/L and in patients with a high risk of progression to hypothyroidism (those with high antibody titers). Because of the risk of developing hypothyroidism, patients with a history of chronic lymphocytic thyroiditis require annual assessment of thyroid function.

### Invasive Fibrous Thyroiditis (Riedel's goiter)

First described by Riedel in 1898, this remains the rarest type of thyroiditis. In addition to the development of dense fibrosis of the thyroid gland itself, extracervical sites of fibrosis frequently occur as inflammatory fibrosclerotic processes, including sclerosing cholangitis, retroperitoneal fibrosis and orbital pseudotumor. Studies suggest that one third of patients with fibrous thyroiditis develop multifocal fibrosclerosis. The mean age at presentation is 47,8 years, and 83 percent of all cases occur in females. A stone-hard or woody mass that extends from the thyroid is common. Symptoms vary according to the structures involved and most commonly result from a thyroid mass that produces dyspnea, dysphagia and, occasionally, stridor. The thyroid mass may grow suddenly or slowly, and is usually unilateral. RAIU is decreased in affected areas of the gland. Most patients remain euthyroid, and the ESR is frequently elevated. Thyroid autoantibodies are present in appreciable quantities in 45 percent of patients. Because of the similarity between fibrous thyroiditis and thyroid carcinoma, diagnosis must be made using open biopsy. The disease is usually self-limited, with surgical wedge resection of the thyroid isthmus being the mainstay of treatment in symptomatic patients.



\*—Graves' disease is not a subtype of thyroiditis.

**Figure 3. Differentiating thyroiditis**  
**Control of initial level of knowledge**

**Task 1.** Which one of iodine-containing hormones of thyroid gland is hormonally inactive?

- a) General  $T_4$       b) Free  $T_4$       c) General  $T_3$       d) Free  $T_3$       e) Reversible  $T_3$

**Task 2.** What dose of thyrodine should be applied in order to begin treatment of hypothyrosis in patient with coronary artery disease?

- a) 0,025 g 1 time a day    b) 0,05 g 1 time a day    c) 1 g 1 time a day    d) 0,1 g 2 times a day

**Task 3.** What disease or state causes the most significant deceleration of Achilles tendon reflex?

- a) Diabetes mellitus    b) Atherosclerosis    c) Hypokalemia    d) Primary hypothyrosis

**Task 4.** What preparation should be prescribed to a patient with autoimmune thyroiditis in case of the acute enlargement of thyroid gland and the increase of antithyroid antibodies titer?

- a) Thyroxin    b) Prednisolone    c) Suprastin    d) Verapamil

**Task 5.** What assay helps to perform the differential diagnosis between primary and secondary hypothyrosis?

- a) Determination of  $T_3$  and  $T_4$  level in blood    b) Determination of TTH in blood    c) Test with thyrotropin-releasing hormone

**Task 6.** What assay helps to perform the differential diagnosis between secondary and tertiary hypothyrosis?

- a) Determination of TTH in blood    b) Test with thyrotropin-releasing hormone

**Task 7.** The tissue sensitivity to the thyroid hormones is the most significant in case of:

- a) Young age    b) Pregnancy    c) Elderly age    d) Heart failure

**Task 8.** Overdosage of thyroid hormones is accompanied by:

- a) Tremor    b) Hyperexcitability, disorders of sleep    c) Night sweats    d) Weight loss    e) Everything mentioned above

**Task 9.** The most possible complication during delivery in pregnant women with hypothyrosis:

- a) Powerless labor    b) Accelerated labor    c) Bleeding    d) Heart failure

**Task 10.** What are the long-term effects of radioactive iodine isotopes on thyroid gland in case of nuclear reactor disaster?

- a) Thyroiditis    b) Hypothyrosis    c) Thyroid cancer    d) All mentioned above

**Correct answers:**

1	2	3	4	5	6	7	8	9	10
E	A	D	B	B	B	D	D	A	D

**Control of final level of knowledge**

**Task 1.** The syndrome of Schmidt includes:

a) Hypocorticism+hypothyrosis+hypogonadism	c) Hypocorticism + hypogonadism
b) Hypothyrosis+hypogonadism	d) Galactorrhoea + hypothyrosis

**Task 2.** The congenital hypothyroidism is characterized by the increased level of TTH in blood of newborn child during:

- a) 12 hours after birth      b) 24 hours after birth      c) 48 hours after birth      d) More than 48 hours after birth

**Task 3.** The main reason for galactorrhea in patients with hypothyroidism is:

- a) Deficiency of thyroid hormones      b) Excess of TTH      c) Hypersecretion of thyroliberine      d) All mentioned above

**Task 4.** In what cases the increased level of TTH in blood is not a sign of hypothyroidism?

- a) Excessive secretion of TTH by pituitary tumor (thyrotropinoma);  
 b) Ectopic secretion of TTH;  
 c) Newborns up to 48 hours after birth;  
 d) All mentioned above

**Task 5.** What criteria are the most adequate ones for the adjustment of thyroid hormones dose in treatment of Hashimoto's disease?

- a) Normalization of T3      d) Reduction of size and density of thyroid gland  
 b) Normalization of T4      e) Reduction of titer of antibodies to thyroglobulin  
 c) Normalization of TTH

**Task 6.** What is the most important feature of thyroid gland structure according to the results of ultrasonography in case of autoimmune thyroiditis?

- a) Echogenic density increased      d) Heterogeneous echogenic density  
 b) Echogenic density decreased      e) Homogeneous echogenic density  
 c) Echogenic density is not changed

**Task 7.** What type of immunity may be impaired in patients with autoimmune thyroiditis?

- a) Humoral      b) Tissue      c) Both of them

**Task 8.** The main indication for the prescription of thyroxine is:

- a) Primary hypothyroidism      b) Secondary hypothyroidism      c) Tertiary hypothyroidism

**Task 9.** What is the maximal duration of action of thyroxine after its withdrawal?

- a) One day      b) Two days      c) 4–6 days      d) 2–3 weeks      e) 1 month

**Task 10.** What is the most critical period for normal brain development of the child, when the adequate levels of thyroid hormones are incredibly important?

- a) First months after birth      b) First year      c) A period from 3 to 5 years old      d) A period from 5 to 10 years old

**Correct answers:**

1	2	3	4	5	6	7	8	9	10
B	C	A	D	E	C	C	C	D	C

### Test tasks

**Task 1.** What are the most important indications for the appointment of glucocorticoids in case of autoimmune thyroiditis?

- a) Large goiter      b) High density goiter      c) Signs of inflammation      d) The presence of nodules

**Task 2.** All listed below diseases have autoimmune origin, except of:

- a) *Hashimoto's thyroiditis*      b) *Addison's disease*      c) *Nelson's syndrome*

**Task 3.** Which type of therapy is preferred in the treatment of Riedel's goiter?

- a) *Radiation*      b) *Surgical*      c) *Thyroid hormone replacement therapy*

**Task 4.** The most important element of pathogenesis of hypothyroid coma is:

- a) *Depression of the respiratory center of the brain and hypoxia;*  
b) *Progressive decline in cardiac output;*  
c) *Hypothermia and increasing hypocorticism;*  
d) *All mentioned above*

**Task 5.** Early transient postoperative hypothyroidism might be caused by:

- a) *Decrease blood supply of thyroid stump;*  
b) *Excessive removal of the thyroid gland;*  
c) *Autoimmune lesions of thyroid stump*

**Task 6.** Early postoperative hypothyroidism develops:

- a) *During the first 6 months after surgery*      b) *9 months*      c) *12 months*

**Task 7.** Early post-radio-iodine hypothyroidism develops within:

- a) *9 months*      b) *1 year*      c) *2 years*

**Task 8.** The early symptoms of hypothyroidism are:

- a) *Significant weight gain*    b) *Hearing loss*    c) *Bradycardia*      d) *Dryness and flaking of the skin*

**Task 9.** What thyroid drugs should be preferred for the treatment of hypothyroid coma?

- a) *Thyroxine*      b) *Triiodothyronine*      c) *Thyroidine*

**Task 10.** What are the most informative criteria for evaluation of the effectiveness of substitution therapy in case of primary hypothyroidism?

- a) *Cholesterol level*    b) *Achilles tendon*    c) *The level of  $T_3$*     d) *The level of TTH*  
*in blood*      *reflex time*      *and  $T_4$  in blood*      *in blood*

**Correct answers:**

1	2	3	4	5	6	7	8	9	10	11	12
B	B	C	C	B	C	A	A	A	B	B	C

### Control questions:

1. Definition of hypothyroidism (HT).
2. The etiology of HT.
3. Metabolic disorders in HT.
4. Clinical manifestations of HT.
5. Thyroid status in HT.
6. The change of the skin and subcutaneous tissue.
7. Hypothyroid myopathy.
8. Myotonic and myasthenic syndromes in HT.
9. 11 Lesions of peripheral nervous system in HT - polyneuropathy.
10. Psychoemotional disorders in HT .
11. Changes in hearing and articulation in HT .
12. The defeat of the cardiovascular system in HT .
13. «Hypothyroid» heart.
14. Changes in heart rate and blood pressure in HT.
15. Manifestations and causes hydropericardium , polyserositis in HT.
16. Lesions of bones and joints in HT.
17. Lesions of the gastrointestinal tract in HT.
18. Kidney damage in HT.
19. Respiratory dysfunction in HT.
20. Anemia in HT.
21. Endocrine disorders in HT.
22. Changes in the hemogram in HT.
23. Biochemical disorders in HT.
24. Disorders of iodine balance in HT.
25. Radiometry of the thyroid gland and thyroid radioisotope scanning.
26. Changes of hormonal levels and tests with TSH and TRH in primary HT.
27. Changes of hormonal levels and tests with TSH and TRH in secondary HT.
28. Changes of hormonal levels and tests with TSH and TRH in tertiary HT.
29. Determination of peripheral HT.
30. Determination of subclinical HT.
31. Age-related peculiarities of HT.
32. Treatment of hypothyroidism.
33. Description of preparations containing thyroid hormones (thyroxine, triiodothyronine, tyreotom).
34. Definition of thyroiditis (T).
35. Classification of T.
36. Thyroiditis with acute clinical course (acute suppurative, nonsuppurative acute, subacute).
37. Hypothyroidism against the background of autoimmune polyendocrine syndrome.
38. Definition of chronic autoimmune thyroiditis (CAT).
39. Clinical variants of CAT (hypertrophic, atrophic, focal form).
40. Symptoms of compression in CAT.
41. Change in functional status of the thyroid gland.
42. Informative laboratory and instrumental studies in CAT.
43. Immunological studies in CAT.
44. Indicators of iodine balance in CAT.
45. Changes of radiometry and radioisotope scanning in CAT.

46. Sonographic features of CAT.
47. Nodular forms of goiter, definition.
48. Differential diagnosis of nodular forms of goiter.

#### **Practical tasks:**

1. Identify the character of thyroid changes by palpation.
2. Identify the risk factors for HT, possible etiological factors of the disease, assess the adequacy of the diagnostic measures which were applied earlier, evaluate pharmacological history of the patient, identify the main stages of the disease.
3. Substantiate the diagnosis of HT.
4. Identify the complications of HT.
5. Evaluate the results of clinical, laboratory and instrumental investigations.
6. Determine the severity of HT.
7. Perform differential diagnosis of nodular goiter.

#### **FURTHER READING:**

1. Endocrinology and metabolism / ed. by Pinchera. – London: McGraw Hill Int., 2001. – 811 p.
2. Handbook of Physiology. Section 7: Endocrine system. Volume III: Endocrine regulation of water and electrolyte balance / ed. by J.C. S. Fray. – Oxford University press, 2000. – 750 p.
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*Навчальне видання*

# **ЗАХВОРЮВАННЯ ЕНДОКРИННОЇ СИСТЕМИ. ГІПОТИРЕОЗ. КЛАСИФІКАЦІЯ, ДІАГНОСТИКА, КЛІНІКА, ЛІКУВАННЯ. ТИРЕОЇДИТ**

***Методичні вказівки  
для студентів IV курсу***

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