Ministry of Education and Science of Ukraine
V. N. Karazin Kharkiv National University

MANAGEMENT OF A PATIENT WITH GOITER

Methodical recommendations
for the preparation of students of higher education in the 6th year of study in the discipline «Internal Medicine»

Electronic resource

Kharkiv – 2024

UDC 616.441-006.5-07(072)
M 24

Reviewers:

O. M. Korzh – octor of Medical Sciences, Professor, Head of the Department of general practice-family medicine of Kharkiv National Medical University;

L. L. Sherstyuk – Candidate of Medical Sciences, associate professor, acting Head of the department of general practice-family medicine of the medical faculty of V. N. Karazin Kharkiv National University.

Approved for distribution in the Internet by the decision of the Scientific and Methodical Council of V. N. Karazin Kharkiv National University (Protocol № 7 from April 16, 2024)

M 24 **Management** of a patient with goiter : methodical recommendations for the preparation of students of higher education in the 6th year of study in the discipline «Internal Medicine» [Electronic resource] / compilers T. M. Tykhonova, M. Yu. Gorshunska, N. Ye. Barabash, O. O. Vasylenko. – Kharkiv : V. N. Karazin KhNU, 2024. – (PDF 39 с.)

The methodological recommendations outline the main aspects of the management of patients with goiter syndrome, which include diagnosis and differential diagnosis of its individual forms, modern approaches to treatment.

For students of the 6th year to prepare for practical classes in the discipline «Internal Medicine»

UDC 616.441-006.5-07(072)

CONTENT

LIST OF CONVENTIONAL ABBREVIATIONS

AIT	autoimmune thyroiditis
WHO	World Health Organization
DTG	diffuse toxic goiter
MRI	magnetic resonance imaging
MSA	microsomal antigen
NCD	neurocirculatory dystonia
FNA biopsy	fine needle aspiration biopsy
Tg	thyroglobulin
TSH	thyroid stimulating hormone
TPO	thyroid peroxidase
T3	triiodothyronine
Free T3	fine needle aspiration biopsy
T4	thyroxine
Free T4	free thyroxine
US	ultrasound diagnostics
TG	thyroid gland
TI-RADS	Thyroid imaging reporting and data system

INTRODUCTION

Problems with thyroid gland are widespread in many countries. Worldwide, approximately 8 % of the population has goiter. According to the World Health Organization (WHO), thyroid diseases rank second among endocrine disorders after diabetes mellitus. More than 665 million people in the world have endemic goiter or suffer from other forms of thyroid pathology. According to statistics, the increase in the number of thyroid diseases in the world is 5 % per year. Women develop thyroid problems 7–10 times more often than men. The risk of these diseases increases with age for both women and men, and after age 70, the prevalence of subclinical hypothyroidism in men is almost as high as in women. Since thyroid pathology is widespread among people of working age, it is an urgent medical and social problem. Therefore, it is very important to detect thyroid diseases intime and prescribe effective treatment.

1. BASIC KNOWLEDGE, SKILLS, ATTAINMENTS NECESSARY FOR THE TOPIC STUDYING

Names of previous disciplines	Acquired skills
Foreign Language	To be able to work with foreign literature to gain knowledge about modern methods of diagnosis and treatment of endocrine diseases
Medical informatics	Apply modern computer programs and be able to work with them, have statistical methods for processing the results of clinical studies, analyze the results of studies, be able to evaluate and interpret the results of clinical studies given in information sources, be able to work with electronic databases
Human anatomy. Normal physiology. Histology, cytology and embryology	Know the normal anatomy, function and regulation of the hypothalamic-pituitary-thyroid system, understand and be able to evaluate the relationship of its structure and its influence on other organs and metabolic processes in the human body
Pathomorphology. Pathophysiology	Know typical pathological processes: mechanisms of development, changes in the human body, compensatory reactions of the body, the development of connections that have a «cause-and-effect» character. To describe and schematically represent the mechanism of development of typical pathological syndromes in thyroid pathology, to justify pathogenetic approaches to their drug therapy
Propaedeutics of internal medicine	Conduct a physical examination of patients, analyze the results of basic laboratory and instrumental research methods. Identify the leading symptoms and syndromes in diseases of the thyroid gland. To be able to make a differential diagnosis, justify and formulate a diagnosis on the basis of a physical examination and the data of additional methods

Pharmacology	Be able to navigate the nomenclature of medicines used in the therapy of patients with thyroid pathology. Know the mechanism of action of such medicines, their pharmacodynamics, indications and contraindications for their use. Know the peculiarities of the pharmacological action of these drugs in different categories of patients. Make a reasonable choice of individual drugs and therapy schemes in accordance with the principles of evidence-based medicine, optimization of treatment schemes, evaluate the effectiveness and safety of pharmacotherapy taking into account the individual characteristics of the patient, the presence of concomitant diseases

The student should know

- Definition of the concept of goitre syndrome.
- Epidemiology of thyroid diseases in Ukraine.
- Risk factors for the development of various thyroid gland pathologies.
- The mechanism of hormonal and metabolic disorders in these diseases.
- Etiology and pathogenesis of thyroid diseases.
- Classification of goitre.
- Spectrum of iodine deficiency diseases and methods of iodine prevention and iodine therapy.
- Laboratory diagnosis of thyroid pathology, namely: markers of functional state, tumor markers and markers of autoimmune destruction.
- Clinical picture of diseases accompanied by goitre syndrome, their diagnostic criteria.
- Indications for conducting and the basis of the results interpretation of hormonal studies and tests.
- Diagnostic value of ultrasound examination (US) of the thyroid gland, radioisotope examination of the thyroid gland (radiometry, scanning).
- Choosing a method of treatment of diseases of the thyroid gland.

The student should be able

- Identify risk factors for the development of thyroid diseases.
- Diagnose these diseases.
- Determine the degree of thyroid enlargement.
- Determine the degree of severity of the course of thyroid pathology.
- To determine the nature of multiorgan complications of diseases accompanied by goitre syndrome.
- Analyze the results of hormonal studies and functional tests.
- Conduct differential diagnosis of thyroid function disorders among themselves and with other pathologies.
- To evaluate the dynamics of the thyroid status of patients against the background of the use of thyrostatic drugs or thyroid hormones.
- Be able to adjust the dose of thyrostatic drugs and hormone replacement therapy as the euthyroid state is achieved in patients with thyrotoxicosis and hypothyroidism, respectively.
- To draw up a long-term plan for the treatment of thyroid diseases and their complications, to know the technology of involving the patient in participation in the treatment process.
- To be able to choose the tactics of treatment of a patient with thyroid nodules, thyroiditis.

2. TOPIC CONTENT

2.1. Concept of goiter

Goiter- a term denoting a pathological increase in the thyroid gland without specifying its functional state.

Palpation of the thyroid gland is one of the main methods of clinical diagnosis of goiter, but it does not provide an opportunity to quantitatively determine its volume. Thyroid volume is determined by US. The norm for men is the volume of the thyroid gland from 9 to 25 ml, for women 9–18 ml. If, according

to the examination, an increase in the thyroid gland is found without a change in its structure, the term diffuse goiter is used. When neoplasms (so-called nodes) of the thyroid gland are detected, a nodular goiter is diagnosed. The term mixed goiter (or diffuse-nodular) is used when a general increase in the thyroid gland is combined with neoplasms. Thus, according to the structure, goiters are divided into:

- diffuse;
- nodular;
- mixed (diffuse-nodular).

Etiopathogenetic classification of the goitre:

- Endemic goiter – observed in geographical areas with iodine deficiency in the environment.
- Sporadic goiter – observed in non-endemic areas (with physiological provision of iodine).

According to localization, the following are distinguished:

- cervical;
- transthoracic;
- partially retrosternal;
- goiter of the tongue root.

According to the functional state, goiter can be:

- hyperthyroid - increased thyroid function;
- euthyroid - thyroid function is not impaired;
- hypothyroid - thyroid function is reduced.

Both diffuse, nodular, and mixed goiter can be with normal or impaired thyroid function.

The classification adopted in 2001 by the WHO is currently used to assess the degree of thyroid enlargement (Table 1).

Table 1

Classification of goiter sizes (WHO, 2001)

Degree	Description
0	There is no thyroid enlargement (the volume of the lobes does not exceed the volume of the distal phalanx of the patient's thumb)
I	Thyroid enlargement is palpable, but not noticeable when the neck is in a normal position (the lobes are larger than the distal phalanx of the thumb).
II	An increase in the thyroid gland is palpable and clearly determined by the eye when the neck is in a normal position.

The presence of a goiter in a patient indicates thyroid pathology. Therefore, if during the examination of the patient the doctor has suspicions about its presence, the patient needs a thorough clinical, laboratory and instrumental examination (Fig. 1, 2).

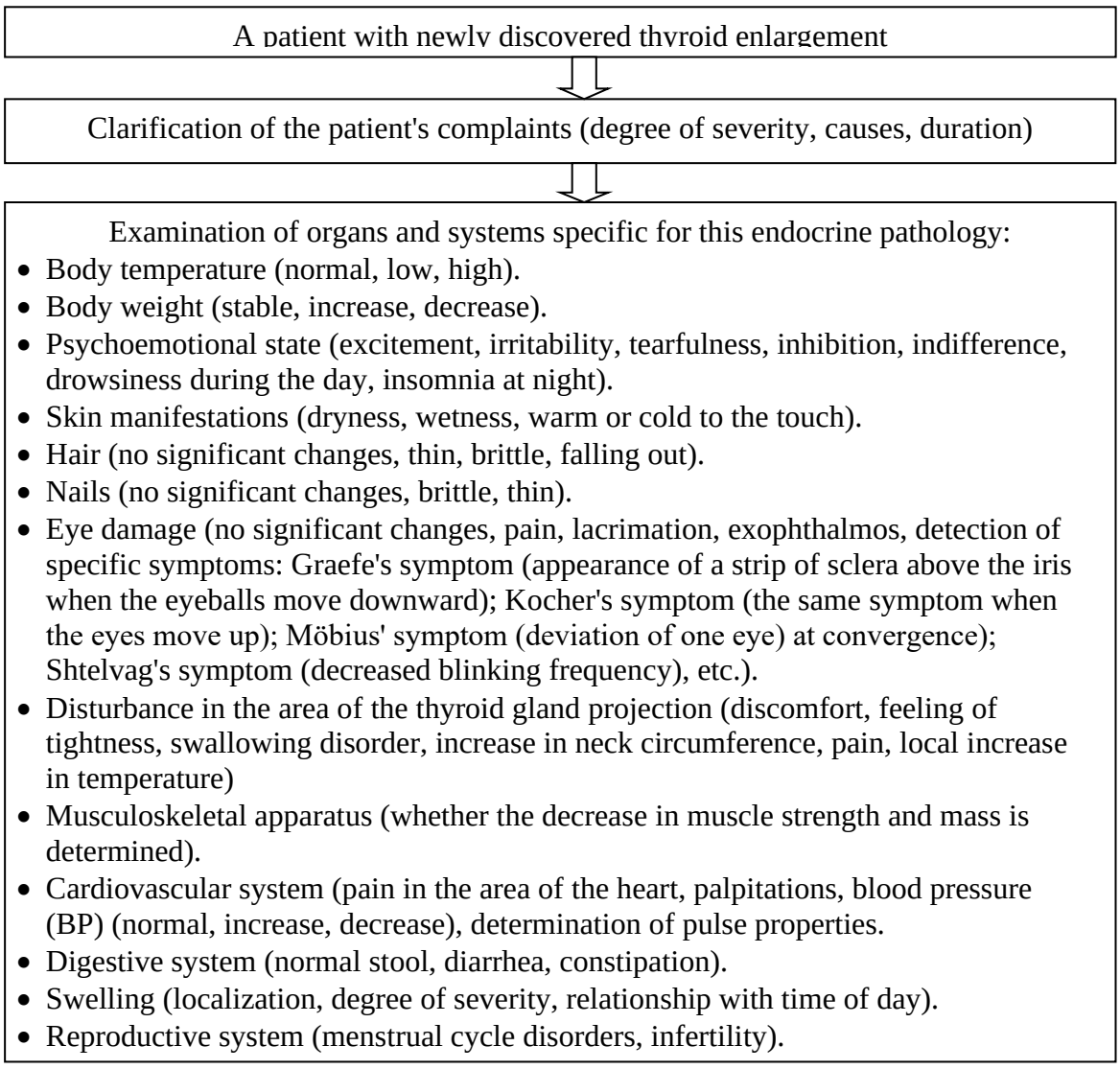

Fig. 1. Patient clinical treatment plan

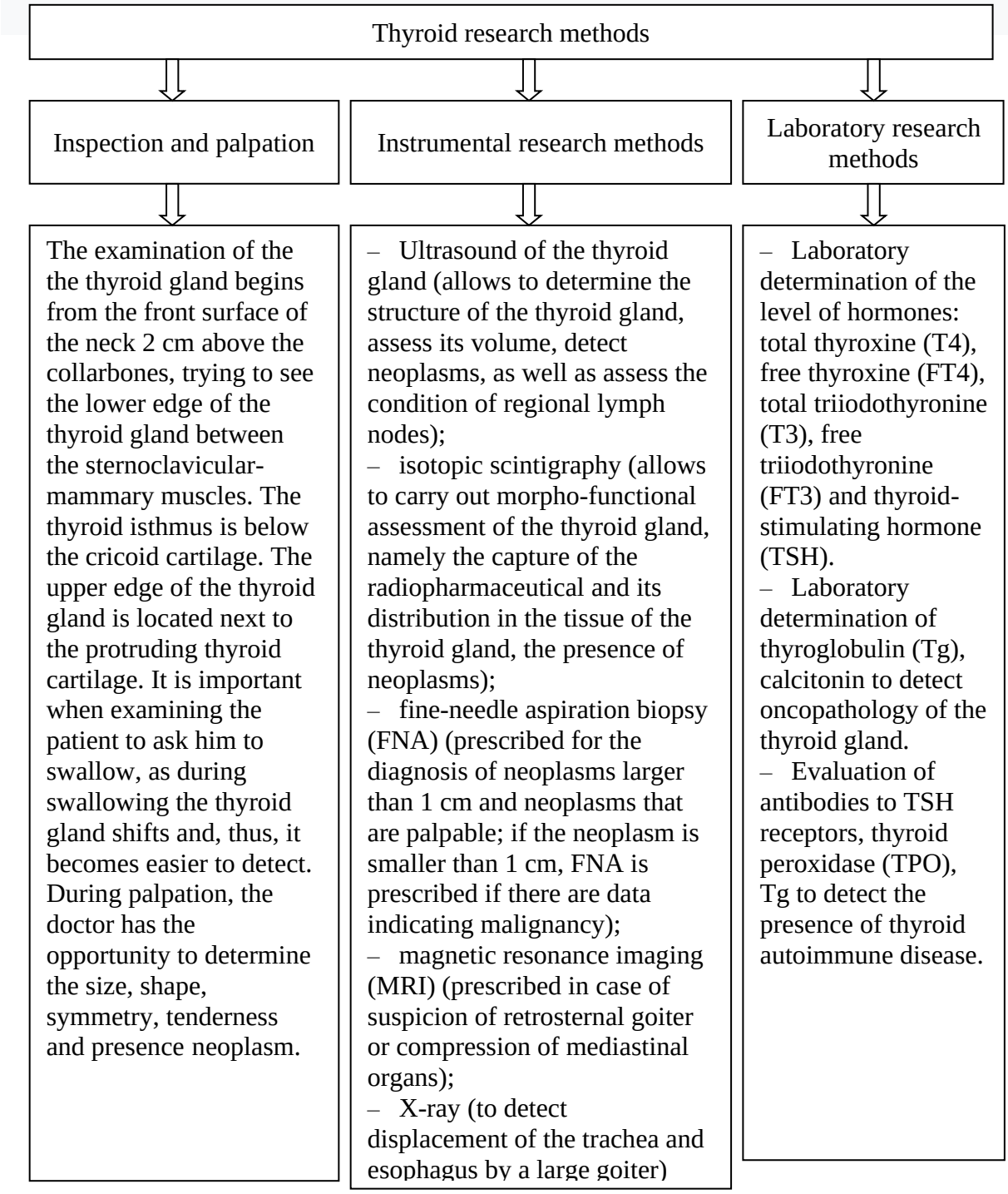

Fig. 2. Methods of thyroid gland research

With regard to laboratory diagnostics, it should be noted that it is better not to determine the total fractions of thyroid hormones (T3, T4), but free (FT3, FT4) in the patient, since it is known that the indicators of the total fractions of hormones in the blood can be reduced in the presence of diseases that are accompanied by loss of a large amount of protein (nephrotic syndrome, systemic

diseases, Cushing's syndrome), and when taking large doses of anabolic steroids and glucocorticoids. An increase in the total fractions of thyroid hormones is observed during pregnancy, taking estrogens, mental illnesses, as well as in some liver diseases.

It is necessary to pay attention to the fact that structural changes of the thyroid gland are not always accompanied by a violation of its function, just as a violation of the function of the gland can be accompanied by minimal changes during US examination.

2.2. Iodine deficiency diseases

As mentioned above, according to the etiopathogenetic principle, goiter is divided into sporadic and endemic. The latter is the main consequence of iodine deficiency in the environment. At the same time, the spectrum of iodine deficiency diseases is quite wide and depends on the period of life in which these diseases manifest (Table 2).

Table 2

Spectrum of iodine deficiency diseases manifestations

Period of life	Possible manifestations
Fetus	Death Developmental disorders
Newborn	Low birth weight Congenital anomalies Frequent development of infectious diseases Hypothyroidism
Children and teenagers	Endemic goiter Hypothyroidism Disorders of mental and physical development Disorders of the formation of reproductive function
Adults	Endemic goiter Hypothyroidism Decreased physical and intellectual capacity
Women of childbearing age	Endemic goiter Anemia Infertility Miscarriage Premature birth The risk of having a child with mental retardation

It should be emphasized that the degree of severity of iodine deficiency is not assessed in each individuals, but is determined in people living in a certain area, based on the study of the prevalence of goiter (by palpation and/or US) and the concentration of iodine in urine.

In order to overcome iodine deficiency, methods of individual, group and mass iodine prophylaxis are used. Individual iodine prophylaxis consists in the consumption of foods with a high content of iodine (sea fish, seafood), as well as medicines that provide a physiological amount of iodine (potassium iodide daily after meals) (Table 3).

Table 3

Recommended doses of potassium iodide at different periods of life

Period of life	Recommended dose of potassium iodide
Children under 12 years of age	50–100 mcg per day
Teenagers and adults	100–200 mcg per day
Pregnant and lactating women	250 mcg per day

Group iodine prophylaxis involves the appointment of iodine medications under the supervision of specialists in groups at the highest risk of developing iodine deficiency diseases (children, adolescents; pregnant and lactating women; persons of childbearing age; persons temporarily living in an endemic goiter region; with a positive family history; patients , who have completed the course of treatment for endemic goiter), especially in organized groups (kindergartens, schools, boarding schools).

Mass iodine prophylaxis is considered the most effective and economical method and is achieved by adding iodine salts (iodide or potassium iodate) to the most common food products (table salt, bread, water) and is designed for all residents of a certain endemic region.

2.3. Hypothyroid goiter

Hypothyroidism is decrease in thyroid function. Persistent deficiency of thyroid hormones leads to changes in the functioning of organs and systems. Hypothyroidism syndrome can be primary, secondary, tertiary and peripheral.

Primary hypothyroidism occurs for a number of reasons.

I. Congenital.

- Thyroid hypoplasia or aplasia.
- Congenital defects in the synthesis of thyroid hormones.

II. Acquired.

- Postoperative.
- Treatment with radioactive iodine and ionizing thyroid irradiation.
- Inflammatory thyroid diseases (thyroiditis).
- Iodine deficiency in the body (in combination with endemic goiter).
- Taking some drugs on a permanent basis (most often thyrostatics).
- Long-term use of hormonal drugs (glucocorticoids, sex hormones) or sulfonamides.
- Neoplastic processes in the thyroid gland.

Currently, the most common cause of primary hypothyroidism is chronic autoimmune thyroiditis. With it, there is an increase in the titer of circulating autoantibodies to the thyroid tissue (antibodies to TPO, to Tg), their reaction with the corresponding cellular antigens occurs, with further development of destructive and proliferative processes, and as a result, a decrease in the production of thyroid hormones.

Secondary hypothyroidism occurs as a result of damage to the pituitary zone and a decrease in TSH secretion:

- ischemia of the adenohypophysis due to massive bleeding during trauma or childbirth;
- inflammatory processes in the brain;
- brain tumor;

– long-term use of drugs such as levodopa, parlodel (bromocriptine), reserpine and others;
– autoimmune damage to the pituitary gland.

Tertiary hypothyroidism occurs as a result of damage to the hypothalamus and a decrease in the secretion of thyroliberin:
– inflammatory processes in the area of the hypothalamus;
– cranial brain injuries;
– brain tumors;
– use of serotonin preparations.

Peripheral hypothyroidism develops as a result of a decrease in the sensitivity of peripheral tissues to thyroid hormones, the provoking factors of which can be:
– the presence of antibodies to thyroid hormones;
– hereditary decrease in the sensitivity of receptors of thyroid-dependent peripheral tissues to thyroid hormones;
– selective resistance to T4;
– violation of the conversion of T4 to T3 in the kidneys and liver.

Understanding the anatomical and physiological features of the functioning of the hypothalamic-pituitary-thyroid system is necessary to establish the correct diagnosis in a patient with newly discovered hypothyroidism (Table 4).

Table 4

Differential diagnosis of various forms of hypothyroidism

Indicator	Primary hypothyroidism	Secondary hypothyroidism	Tertiary hypothyroidism
TSH	↑	↓	↓
FT4	↓ or norm	↓	↓
FT3	↓ or norm	↓	↓
Thyroxine-binding ability of proteins	↑	↑	↑
The ^{131}Iodine Thyroid Uptake	↓	↓	↓

Depending on clinical and laboratory indicators, primary hypothyroidism is divided into subclinical and manifest (obvious). Subclinical hypothyroidism has no clinical symptoms and is accompanied by an isolated increase in the TSH level > 4 mIU/ml (but less than 10 mIU/ml) without any changes in the levels of thyroid hormones.

Severity of hypothyroidism (mild, moderate, severe) are determined by the severity of clinical manifestations. With a mild degree (subclinical hypothyroidism), the clinical picture is absent or not pronounced, TSH ≤ 10 mIU/l, T4 is normal. With a moderate degree of severity, the clinical picture is pronounced, TSH > 10 mIU/l, T4 ↓. In severe cases, in addition to the clinical and laboratory signs of manifest hypothyroidism, its complications are presented. Assessment of the degree of severity of the disease should be carried out after reaching the maximum compensation of the patient's condition.

The main difficulties in the diagnosis of hypothyroid goiter are the high prevalence of similar symptoms in other somatic and mental diseases. Therefore, when making a diagnosis, one should always remember the so-called «masks» of the hypothyroidism syndrome (Fig. 3, Tables 5–7).

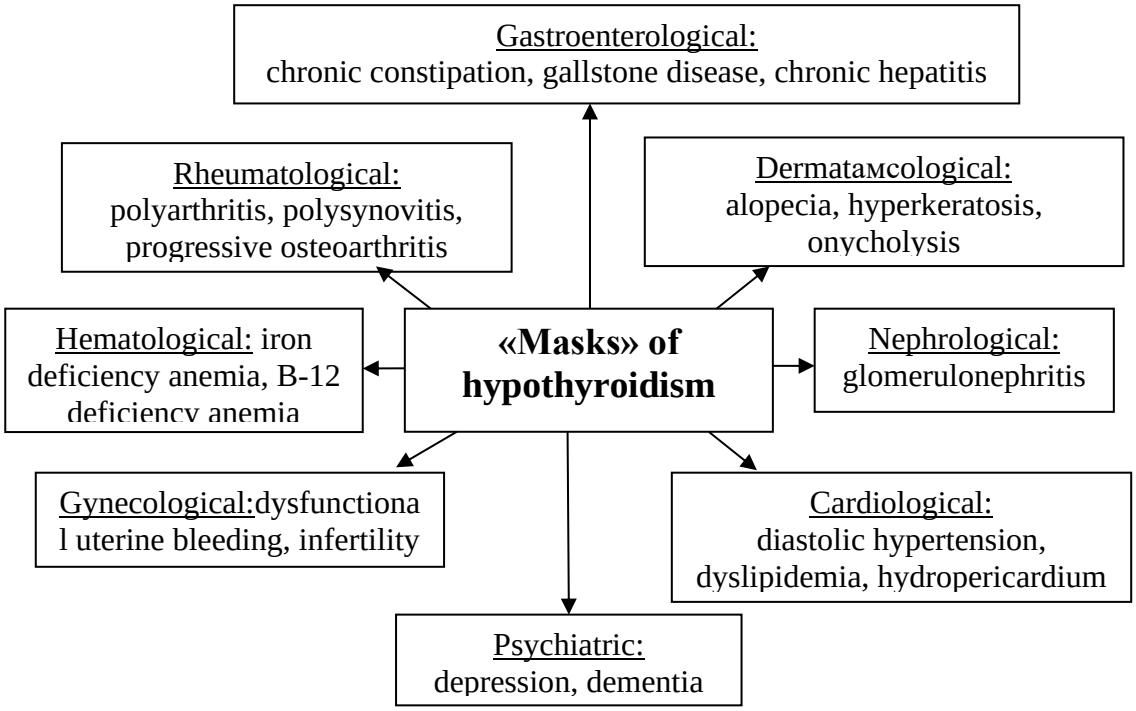

Fig. 3. «Masks» of hypothyroidism

In order to clarify the diagnosis and prescribe the correct therapy, it is necessary to carry out a differential diagnosis of hypothyroidism syndrome with other non-endocrine conditions. For example, a decrease in T3 is found in coronary heart disease and angina pectoris; a decrease in T4 is sometimes found in intensive care patients and patients who are on constant glucocorticosteroids.

Table 5

Differential diagnosis of hypothyroidism and glomerulonephritis

Indicator	Hypothyroidism	Chronic glomerulonephritis
Chilliness	Yes	No
Inhibition	Yes	No
Drowsiness	Yes	No
Headache	No	Yes
Memory	reduced	normal
Hair loss	Yes	No
Skin	dry with slight flaking, cold to the touch with a waxy tint	pale, not cold; mild peeling and dryness in chronic renal failure
Swelling	generalized, dense, do not change during the day, no pit remains after pressure	mild swelling, more often on the face and lower limbs, more pronounced in the morning and evening
Pulse	bradycardia	more often normocardia, tachycardia is possible
Blood pressure	more often it is lowered, but it can be both normal and elevated	increased
General analysis of urine	slight proteinuria is possible	proteinuria, cylindruria, hematuria
Decrease in indicators of T3, T4	Yes	No
Effectiveness of taking thyroid hormones	Yes	No

Table 6

Differential diagnosis of hypothyroidism, iron-deficiency and B12-deficiency anemia

Indicator	Hypothyroidism	Iron deficiency anemia	Anemia B12-deficient
Swelling, pastiness of the face	Yes	No	No
Skin	pale with a waxy tint, dry, cold to the touch	pale, not cold	pale yellowish, not cold
Drowsiness, adynamia	Yes	No	No
Pulse	bradycardia	tachycardia	tachycardia
Hydropericardium (with echography)	Yes	No	No
Complete blood test	hypochromic anemia, increased ESR, lympho-cytosis, tendency to leukopenia	hypochromic anemia, poikilocytosis, anisocytosis	normochromic or hyperchromic anemia, macrocytosis, hyper-segmented neutrophils, tendency to leukopenia
Hepatosplenomegaly	No	No	Yes
Blood iron indicators	Normal or slight decrease	reduced	norm
Myelogram	without significant changes	reduced number of sideroblasts	in a large number of megaloblasts
Decrease in blood T3, T4 indicators	Yes	No	No
An effective method of therapy	Prescribing of thyroid hormones	Prescribing of iron preparations	Vitamin B12 therapy

Table 7

Differential diagnosis of hypothyroidism and heart failure

Indicator	Hypothyroidism	Heart failure
Swelling	Total pastiness, swellings are dense, do not leave a hole when pressed	Swellings are mainly in the area of the lower legs and feet, soft, leave a hole when pressed
Skin	Dry with slight flaking, cold to the touch with a waxy tint	Satisfactory humidity, hands and feet are cold to the touch, cyanotic
Acrocyanosis	No	Yes
Auscultation of the heart	Tones are muffled	Maybe a gallop rhythm
Decrease in blood T3, T4 indicators	Yes	No
An effective method of therapy	Prescribing of thyroid hormones	Prescribing of diuretics, vasodilators, cardiac glycosides

Treatment of hypothyroid goiter

The main task of treatment is to restore the normal physiological functions of all organs and systems, which have been disturbed due to hypothyroidism. With any form of hypothyroidism, the basis of treatment is adequate replacement therapy with levothyroxine (L-thyroxine) drugs. Estimated daily dose for manifest hypothyroidism is 1.6–1.8 mcg/kg in patients under 55 years of age, the initial dose is 25–50 mcg/day with a further increase of 25–50 mcg every 5–7 days. In patients with concomitant diseases of the cardiovascular system and older than 55 years, the daily dose is lower – 0.9 μg/kg of weight. Their initial dose is 12.5–25 mcg/day with subsequent dose increases of 12.5–25 mcg every 6–8 weeks. The criterion of treatment adequacy is the disappearance of clinical and laboratory manifestations of hypothyroidism.

In some cases, when therapy with maximal or submaximal doses of L-thyroxine (about 200 μg) is ineffective, triiodothyronine drugs are prescribed, the maximum therapeutic dose of which reaches 200–300 μg/day, or combined triiodothyronine and levothyroxine drugs (novotiral (20/100), Thyreotom (10/40)).

In most cases, improvement in the general condition of a patient with hypothyroidism begins in the first week after taking the drug. Complete disappearance of clinical symptoms usually occurs within several months. In elderly people and weakened patients, the reaction to the drug develops more slowly. It is recommended to control the adequacy of the dose once every 4–6 weeks by determining TSH level. The normal level of TSH is 0.4–4.0 μU/ml, in pregnant women the upper limit of normal is 2.5 μU/ml, for elderly patients the limits of normal TSH values are not so strict.

It should be noted that most often hormone replacement therapy is prescribed for life, as it is extremely rare to observe the restoration of thyroid hormone function to a euthyroid state.

2.4. Hyperthyroid goiter

The terms «hyperthyroidism» and «thyrotoxicosis» are not identical. Hyperthyroidism is increased secretion of thyroid hormones due to hyperfunction of thyroid gland, which exceeds the actual need of the body and leads to the development of a specificic symptom complex. Thyrotoxicosis is a syndrome in which there are clinical and biochemical manifestations of an excessive content of thyroid hormones in the blood, regardless of the reason for the increase in their level, in particular, the production of hormones: functionally active metastases of follicular cancer of the thyroid gland, struma ovarii (tumor of the ovaries), chorioepithelioma, as well as against the background of overdose of thyroid hormones (iatrogenic thyrotoxicosis), amiodarone-induced thyrotoxicosis. In most cases, thyrotoxicosis develops as a result of hyperthyroidism.

The syndrome of thyrotoxicosis, as well as the syndrome of hypothyroidism, can be primary, secondary and tertiary. Primary thyrotoxicosis is caused by the pathology of the thyroid itself, secondary thyrotoxicosis occurs as a result of damage to the pituitary zone, tertiary thyrotoxicosis develops when the hypothalamus is damaged.

Depending on the source of excess secretion of thyroid hormones, thyrotoxicosis has several forms.

1. Diffuse toxic goiter (DTG) (Graves' disease, Basedow’s disease). This is a systemic autoimmune disease that develops against the background of the production of antibodies to TSH receptors and is the cause of thyrotoxicosis in 80–85 % of cases. Diagnostic criteria are the following:

- clinical signs of thyroid hyperfunction;
- increase in thyroid function (↑ FT3, ↑ FT4, ↓ TSH);
- presence of diffuse thyroid tissue changes with increased blood flow according to ultrasound data;
- increased level of antibodies to TSH receptors.

2. Thyrotoxic adenoma. It is characterized by thyrotoxicosis syndrome in the presence of thyroid adenoma, which produces thyroid hormones in excess. Thyrotoxic adenoma functions autonomously, i. e. excess production of hormones is not regulated by hypothalamic-pituitary-thyroid relations. This disease is more common in women over 40 years of age.

3. Destructive thyroiditis (subacute thyroiditis, thyrotoxicosis in autoimmune thyroiditis (AIT), postpartum thyroiditis, painless thyroiditis). This group of diseases is associated with the destruction of thyroid tissue for one reason or another and the release of excess thyroid hormones into the blood. It is diagnosed in the presence of clinical and laboratory signs of thyroid hyperfunction and symptoms of the corresponding thyroiditis.

4. Iatrogenic thyrotoxicosis is a condition caused by an overdose of drugs, in particular, thyroid hormones, in the treatment of hypothyroidism. This group of diseases can also include *cordarone-induced (amiodarone-induced) thyrotoxicosis*, which occurs as a result of treatment with antiarrhythmic drugs cordarone (amiodarone) due to an excess of iodine in them (the so-called iodine-Basedow's). Taking of these drugs causes the destruction of thyroid cells, followed by the release of excess thyroid hormones into the blood.

5. Multinodular toxic goiter. It develops in older people, about 50–60 years old. An excess of thyroid hormones is observed due to the hyperfunction of thyroid nodes.

6. Thyrotropinoma- this is a neoplasm of the pituitary gland that excessively synthesizes TSH, which stimulates the production of thyroid hormones by the thyroid gland. It is a very rare disease. Diagnostic criteria:

- clinical signs of thyroid hyperfunction;
- increased thyroid function due to hyperproduction of TSH (↑ FT3, ↑ FT4, ↑ TSH).

For the purpose of correct diagnosis and timely detection of thyrotoxicosis syndrome, it is recommended firstly check the level of such hormones as TSH and FT4 (Table 8).

Table 8

Forms of hyperthyroid (thyrotoxic) goiter

Form	TSH	FT4	Clinical manifestations
Subclinical	Reduced	Norm	Absent
Manifest	Pronounced reduced	Increased	Specific symptoms

Degrees of severity of thyrotoxicosis (mild, moderate, severe) are determined by the severity of disease symptoms, the level of body weight loss, as well as the presence of cardiovascular and nervous system pathology.

The main difficulties in the diagnosis of thyrotoxic goiter are the prevalence of similar symptoms in other somatic and mental diseases. Therefore, when making a diagnosis, you should remember about the so-called «masks» of thyrotoxicosis (Fig. 4).

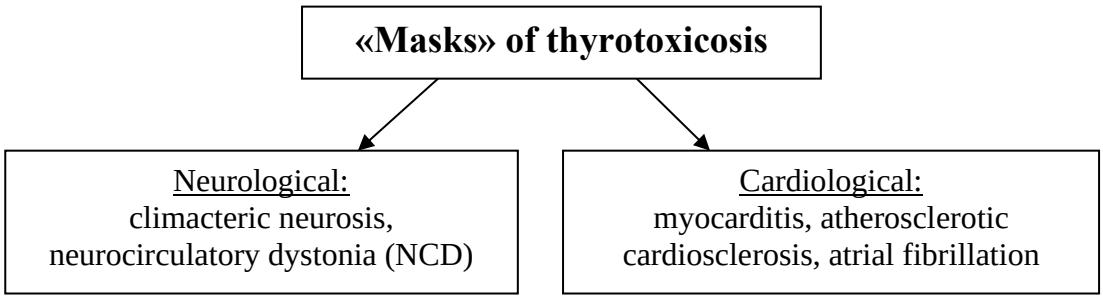

Fig. 4. «Masks» of thyrotoxicosis

In addition, an increase in T4 level can accompany other diseases such as cirrhosis of the liver, viral hepatitis and mental disorders. Differential diagnosis of thyrotoxicosis syndrome, in particular, DTG, is most often carried out with NCD, climacteric neurosis (Table 9), cardiosclerosis and myocarditis (Table 10) due to the similarity of some clinical manifestations.

Table 9

Differential diagnosis of DTG and neurosis

Signs	DTG	NCD	Climacteric neurosis
Sweating	Constantly	Not constantly	Not constantly
Headache	Not typical	Typical, not constantly	Typical, not constantly
Nervous and mental excitement	Psycho-emotional lability, constant irritability	Irritability	Irritability
Body weight	Always pronounced decline	Unchanged	Unchanged
Pain in the heart area	Not typical	Typical	Typical
Tachycardia	Permanent form	Inconstant	Attack-like
Blood pressure	Systolic-increased, diastolic-decreased	More often the norm	More often elevated
Increase of thyroid gland	Typical	Not typical	Not typical
Exophthalmos	Typical	Not typical	Not typical
Blood cholesterol	Decrease	Norm	Norm
T3, T4 level	High	Norm	Norm

Table 10

Differential diagnosis of DTG and heart diseases

Signs	DTG	Myocarditis	Cardiosclerosis with atrial fibrillation
Anamnesis	DTG are often hereditary	Often manifests after a streptococcal or viral infection	Frequent attacks of angina pectoris, myocardial infarction in the past
Age of the patient	Middle	Young	Elderly people
Tachycardia	Permanent form	During physical exertion	During physical exertion
Pain in the heart area	Not typical	Possible, dull, aching. Nitrates are ineffective	During physical exertion. The effect of nitrates taking
Body mass	Always pronounced decline	Weight loss is rare	Not typical
Swelling	With severe course	Possible in the evening	Both permanent and only in the evening are possible
Symptoms of neurosis	Typical	Not typical	Not typical
Increase of thyroid gland	Typical	Not typical	Not typical
Exophthalmos	Typical	Not typical	Not typical
Heart tones	Loud	Weakened	Weakened
Level T3, T4	Increased	Norm	Norm
Cholesterol level	Reduced	Norm	Increased

When carrying out a differential diagnosis, one should also remember the possibility of atypical variants of the thyrotoxicosis course. Depending on the predominance of one or another symptomatology, the following atypical forms are distinguished: lipodystrophic, cachectic, apathetic, neuropsychiatric, neuromuscular, gastrointestinal, cardiovascular and «obese Basedow».

Treatment of hyperthyroid goiter

The main goal of the treatment of thyrotoxicosis is to achieve an euthyroid state and prevent the development of complications (Fsg. 5).

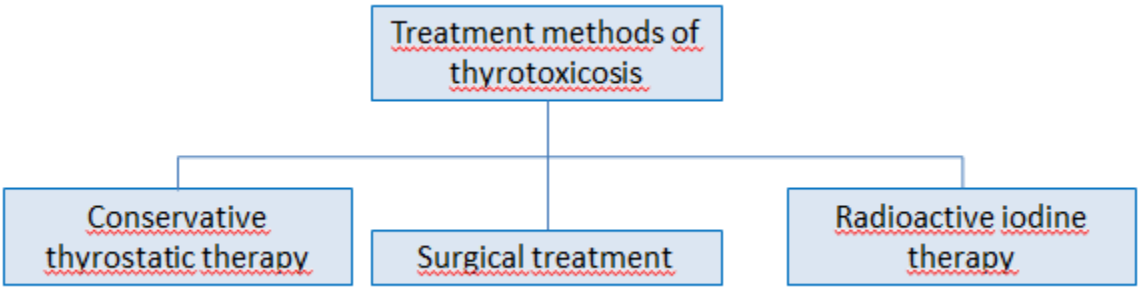

Fig. 5. Treatment methods of thyrotoxicosis

The choice of treatment method depends on the cause and severity of the disease, the size and location of the goiter, the presence of endocrine ophthalmopathy, complications and concomitant diseases, the practice that has developed in different countries, the geophysical features of the area (presence of iodine deficiency), the age and wishes of the patient.

1. ***Conservative thyrostatic therapy*** thiourea derivatives (thiamazole, methimazole, carbimazole) and propylthiouracil (propicyl). Treatment with thiourea derivatives begins with a dose of 30–40 mg/day with a gradual reduction by 5 mg once every 10–14 days under the supervision of a doctor (the rate of dose reduction depends on the clinical and laboratory «reaction» of the patient to treatment) until reaching a maintenance dose of 2,5–10 mg/day. This group of drugs has a possible side effect in the form of leukopenia, therefore, every 10–14 days before reaching the maintenance dose, the patient should monitor the complete blood test. Propylthiouracil therapy is carried out according to the same

scheme with an initial dose of 300–400 mg/day, the maintenance dose is 50–100 mg/day.

The duration of conservative treatment with thyrostatic agents is 12–24 months without a break, with constant monitoring of the patient's general condition and the level of thyroid hormones once every 4–6 weeks. Against the background of thyrostatic drugs, the development of hypothyroidism is possible, which is not a reason to stop therapy, since premature withdrawal of the such medications will lead to a recurrence of thyrotoxicosis. In this case, the dose of the thyrostatic drugs is reduced to the maintenance level and levothyroxine (25–75 mcg/day) is added. This scheme of treatment was called «block and replace».

It should be taken into account that the risk of recurrence of thyrotoxicosis increases with:

- smoking;
- in men;
- with a large goiter;
- ↑ level of antibodies to TSH receptors.

2. *Surgical treatment*

Indications for surgical treatment:

- the presence of thyroid neoplasms;
- large goiter sizes (volume over 45 ml) and in the presence of signs of compression of adjacent organs;
- severe thyrotoxicosis regardless of size;
- retrosternal location of the goiter;
- recurrences of thyrotoxicosis after conservative therapy or treatment inefficiency;
- intolerance to thyrostatic drugs.

In order to prevent a thyrotoxic crisis in the postoperative period, surgical treatment is performed only after the patients reach an euthyroid state. For this purpose, in addition to the above mentioned conservative thyrostatic therapy, to

speed up the effect, it is also possible to prescribe Lugol's solution per os (treatment begins with 3–5 drops 3 times a day after meals (diluted with milk or water), every day the dose is increased by 1 drop with each intake, bringing it to a maximum of 15–20 drops 3 times a day). The principle of using Lugol's solution is directly related to the Wolff-Tchaikov effect, which consists in the fact that excessively large doses of inorganic iodine can lead to an initial increased formation of thyroid hormones with subsequent inhibition of this process.

As a rule, with thyrotoxicosis, a subtotal resection of the thyroid gland is performed, leaving no more than 2–3 ml of its tissue. In this case, postoperative hypothyroidism develops, so patients need life-long levothyroxine replacement therapy, starting from 7th days after surgery.

3. *Radioactive iodine therapy*

The principle of treatment with radioactive iodine is based on the fact that thyroid tissue absorbs and retains radioactive iodine, which β-radiation destroys thyroid tissue. The radioactive iodine is taken orally in the form of sodium salt 131J in a solution or capsule. The dose of therapy is determined individually.

Indications for radioactive iodine therapy:

- Moderate or severe DTG in patients over 40 years of age with no effect from long-term thyrostatic drugs treatment;
- severe concomitant diseases (myocardial infarction, recent stroke, hypertensive crisis, etc.), when surgical treatment is impossible and drug therapy is ineffective;
- severe forms of thyrotoxicosis with severe circulatory failure, toxic hepatitis, psychosis;
- refusal of surgical treatment in the absence of an effect from properly conducted antithyroid therapy;
- recurrence of thyrotoxicosis after surgical treatment of DTG;
- allergic reaction to thyrostatics.

Absolute contraindications are pregnancy and lactation.

2.5. Thyroiditis

The term «thyroiditis» unites several thyroid diseases with different etiology and pathogenesis. Classification of thyroiditis:

1. Acute (purulent, bacterial) thyroiditis.
2. Acute non-purulent thyroiditis.
3. Subacute thyroiditis (De Quervain's, viral, giant cell, granulomatous).
4. AIT (Hashimoto's thyroiditis).
5. Invasive fibrous thyroiditis (Riedel).
6. Chronic specific thyroiditis.

Acute purulent thyroiditis occurs rarely, has an acute course with laboratory signs of bacterial infection, but, as a rule, without any thyroid function impairment. Given the etiology of the disease, treatment is carried out with antibiotics. When an abscess occurs, it is opened, and in case of significant destruction of the part of the thyroid gland, it is promptly removed.

Acute non-purulent thyroiditis occurs rarely due to the action of ionizing radiation. It has an acute course with an increase in body temperature, pain in the thyroid gland and clinical and laboratory signs of thyrotoxicosis. Treatment includes glucocorticoids, β-blockers and thyrostatics.

Subacute thyroiditis occurs acutely, most often after a viral infection, is accompanied by the destruction of thyrocytes. The clinical symptoms include general signs of viral diseases and local symptoms (difficulty swallowing, signs of inflammation in the thyroid gland). Lymphocytosis, an increase in the sedimentation rate of erythrocytes, and clinical and laboratory signs of thyrotoxicosis are also observed. The further evolution of subacute thyroiditis is characterized by the gradual restoration of thyroid function and the change of signs of its hyperfunction to transient hypothyroidism.

Differential diagnosis.This disease differs from acute thyroiditis in the absence of leukocytosis with a shift of the leukocyte formula to the left, as well as a decrease in uptake of radioactive iodine during scanning. The latter also helps

to distinguish subacute thyroiditis from DTG, in which a «hot» zone is observed. The painful variant of Hashitoxicosis (thyrotoxicosis caused by AIT) differs from subacute thyroiditis by the presence of an increased titer of autoantibodies (to Tg, TPO, the microsomal fraction of the follicular epithelium (MSA)), uneven absorption of radioactive iodine, in another words, the absence of a «cold» zone.

Treatment of subacute thyroiditis includes prednisolone 30–40 mg/day for 2–3 weeks followed by a gradual dose reduction of 5 mg/week until complete withdrawal. A good effect from glucocorticoids is also a differential diagnostic feature of subacute thyroiditis. With a milder course of the disease, non-steroidal anti-inflammatory drugs can be used instead of glucocorticoids. Thyrostatic drugs are not prescribed in the thyrotoxic phase of subacute thyroiditis. The use of β-adrenoblockers in most cases is sufficient to relieve the symptoms of thyrotoxicosis.

AIT- chronic inflammatory process in the thyroid gland of autoimmune genesis. It can be hypertrophic (with an increased thyroid volume) and atrophic (with a reduced thyroid volume), in terms of clinical course – clinically expressed and latent. AIT does not have a specific clinical picture. The diagnosis of AIT is based on the presence of palpation signs (diffuse enlargement of the thyroid gland in a hypertrophic form, dense consistency, lobular structure), ultrasound signs (diffuse heterogeneity and decreased echogenicity of the thyroid gland), increased titers of autoantibodies (to Tg, TPO, MSA), often – changes in the functional state of thyroid gland (mainly hypothyroidism). There is no specific treatment for AIT. Changes in thyroid function are treated according to appropriate schemes.

Postpartum thyroiditis (hidden, silent) is considered as a specific form of AIT that develops after childbirth. Disorders of thyroid function have a phase character: usually the disease manifests 8–12 weeks after childbirth with transient hyperthyroidism, which then in most cases passes into a hypothyroid phase. After approximately 6–8 months, patients recover their euthyroid state. Diagnostic criteria for postpartum thyroiditis:

- the connection between the disease and childbirth;
- moderately enlarged, compacted, painless thyroid gland;
- transient thyrotoxicosis in the absence of a high titer of thyrostimulating antibodies (unlike DTG);
- high titer of antibodies to MSA;
- diffuse or multifocal hypoechoic changes at thyroid ultrasound;
- lymphoid infiltration during morphological examination.

Therapy consists of altered thyroid function correction, which is treated according to generally accepted schemes at the stages of the disease's evolution.

Invasive fibrosing thyroiditis (Riedel's) is rare, characterized by massive growth of connective tissue in the thyroid gland and signs of compression of surrounding organs. Riedel's thyroiditis differs from AIT by low titers of autoantibodies in the blood. Unlike thyroid cancer, this disease has a longer course, absence of enlarged regional lymph nodes, diffuse (not regional) thickening of the organ, absence of atypical cells during morphological examination. Treatment of fibrotic thyroiditis is only surgical.

Chronic specific thyroiditis occur against the background of tuberculosis, syphilis, actinomycosis, lymphogranulomatosis, amyloidosis, sarcoidosis, which cause destructive changes in the thyroid gland and lead to hypothyroidism. The diagnosis is established with the help of TAPB. Therapy consists of hormone replacement therapy for hypothyroidism and specific treatment of the underlying disease.

2.6. Nodular goiter

Neoplasms of the thyroid gland (so-called nodes) can be detected during palpation of the neck, but most often they are detected accidentally, during the examination of the neck organs for other indications, for example, during sonography of the carotid arteries. In the case of their detection, an urgent task is

to differentiate benign thyroid nodules from malignant tumors. The most widely used ultrasound of the thyroid gland, which allows not only to detect pathological formations on the neck, including nodes and lymphadenopathy, but also to distinguish benign formations from malignant ones by their sonographic characteristics. To unify ultrasound changes, the TI-RADS (Thyroid imaging reporting and data system) classification is widely used today, which allows you to assign a patient to one or another risk class for the presence of malignant forms of nodular goiter and to determine the further tactics of patient management (observation, TAPB, surgical treatment). A certain ultrasound change (set of changes) is assigned 1 point. The sum of conditional points obtained after the ultrasound of the neoplasm allows the patient to be assigned to one of 5 categories (Table 11).

Table 11

Management algorithm of patients with nodular goiter according to the TI-RADS classification

	TI-RADS 1	TI-RADS 2	TI-RADS 3	TI-RADS 4	TI-RADS 5
Scores	0–1 points	2 points	3 points	4–6 points	≥ 7 points
The probability of malignant potential	Benign signs	Absence of suspicious signs	Slight suspicious signs	Moderately suspicious signs	Expressed suspicious signs
Patient management tactics	TAPB is not necessary, observation	TAPB is not necessary, observation	≥ 1.5 cm – observation, ≥2.5 cm – TAPB	≥ 1.0 cm – observation, ≥ 1.5 cm - TAPB	≥ 0.5 cm – observation, ≥1.0 cm – TAPB

TAPB is considered the main method of diagnosing thyroid neoplasms. The procedure is simple, safe and can be performed on an outpatient basis. When performing a puncture biopsy for a nodular goiter, colloid and thyrocytes are usually obtained. The ratio of these components characterizes the type of goiter: if the colloid predominates, it is a colloidal goiter; in the presence of a large

number of thyrocytes – a proliferative goiter. Variants of the results of thyroid nodules cytological findings (Bethesda System, 2009) are divided into 6 classes.

Class 1. Uninformative: samples prepared with technical errors or insufficient amount of material (follicular cells) – cancer risk 1–4 %.

Class 2. Benign: includes colloid or hyperplastic nodules, Hashimoto's or granulomatous thyroiditis, cysts – risk of cancer 0–3 %.

Class 3. Atypia of unclear significance or follicular lesion of unclear significance – risk of cancer 5–15 %.

Class 4. Follicular neoplasia (tumor) or suspicion of follicular neoplasia – risk of cancer 15–30 %.

Class 5. Suspected cancer (specimens that show signs of malignancy but do not contain all the diagnostic criteria for cancer) – risk of cancer 60–75 %.

Class 6. Malignant – risk of cancer 97–99 %.

Patient management algorithm are determined according to the morphological category. Dynamic observation or the different types of treatment are indicated for patients with nodular goiter: conservative treatment (drug), radioiodine therapy, minimally invasive interventions (ethanol sclerotherapy, laser-induced thermotherapy and radiofrequency ablation of thyroid nodules), surgical intervention. The main goal of treatment is to prevent or delay the further growth of the node (the growth of the node during ultrasound examination in dynamics is considered the increase of its diameter by 50 % from the original in 6 months).

Medical treatment is justified in the presence of a colloidal proliferative goiter of small size (not > 2 cm, volume not > 2 cm^2 in young people). For this purpose, L-thyroxine medications (suppress hypertrophy), potassium iodide drugs (suppress hyperplasia), selenium medications (in case of concomitant AIT) are used. Radioactive iodine in the treatment of nodular goiter is indicated in the treatment of toxic adenoma, multinodular toxic goiter after achieving euthyroidism. Minimally invasive interventions can be used as the method of

choice when the operation is associated with a high degree of risk due to concomitant diseases, and as an alternative to the operation for nodular colloid goiter with a cosmetic defect. Indications for surgical treatment in patients with nodular goiter are: cytologically confirmed carcinomas, neoplasms suspicious of malignant nature, cases of complex cytomorphological diagnosis (when the frequency of malignancy in this group reaches 20–30 %), local compression syndrome of the neck organs by large benign neoplasms, transthoracic placement of nodes, thyrotoxicosis in nodular and multinodular goiter of large size, cosmetic reasons. The optimal surgical intervention in case of nodular colloid goiter and bilateral damage to the thyroid gland - thyroidectomy, in case of unilateral damage - hemithyroidectomy.

In patients with benign formations according to the results of TAPB, dynamic monitoring consists of periodic (1 time in 1–2 years) ultrasound of the thyroid gland and determination of the TSH level. In patients with thyroid nodules smaller than 1 cm with suspicious ultrasound signs (who are not included in the risk group for the development of aggressive forms of thyroid cancer), dynamic monitoring consists of periodic (1 time in 6–12 months) thyroid ultrasound examination. If the formation increases by more than 1 cm or the symptoms of aggressiveness of cancer appear, TAPB is indicated.

TEST QUESTIONS ON THE SUBJECT OF THE LESSON

1. Choose the main diagnostic criteria for hypothyroid goiter:
   a. decrease in thyroid function (↑ TSH);
   a. the presence of nodular changes in thyroid tissue according to ultrasound;
   b. generalized edema;
   c. osteoporosis.
2. What medicines can be considered pathogenetic in the treatment of diffuse toxic goiter:
   a. levothyroxine drugs;
   b. triiodothyronine drugs;
   c. thyrostatics;
   d. β-blockers.
3. Monitoring of the levothyroxine dose adequacy at the start of hypothyroidism treatment is recommended to be carried out once per:
   a. 2–3 weeks;
   b. 2–3 months;
   c. 3–4 weeks;
   d. 4–6 weeks.
4. Among the listed, choose the method of choice in the treatment of hyperthyroid goiter in case of inefficiency or impossibility of prescribing thyrostatics:
   a. β-blockers prescribing;
   b. diuretics prescribing;
   c. physiotherapeutic treatment;
   d. radioactive iodine therapy.
5. Treatment with thiourea derivatives begins with a dose:
   a. 30–40 mg;
   b. 2.5 mg;
   c. 5–10 mg;
   d. 10–20 mg.
6. Endocrine ophthalmopathy can occur with:
   a. diffuse toxic goiter;
   b. hypothyroidism;
   c. autoimmune thyroiditis without functional impairment;
   d. acute thyroiditis.
7. The degree of thyrotoxicosis severity is determined according to the following criterion:
   a. the presence of the cardiovascular pathology;
   b. the size of the goiter;
   c. the level of thyroid hormones;

d. presence of exophthalmos.

8. In the treatment of infertility in patients with hypothyroidism, the following are primarily prescribed:
    a. bromocriptine;
    b. vitamin E;
    c. progesterone;
    d. L-thyroxine.

9. With diffuse toxic goiter, TSH secretion:
    a. normal;
    b. depressed;
    c. increased

10. A laboratory indicator of the hypothyroidism treatment effectiveness is:
    a. lowering of the cholesterol level in the blood;
    b. normalization of the glucose level in the blood;
    c. normalization of the Tg level in the blood;
    d. normalization of the TSH level in the blood.

Keys: 1) – a; 2) – c; 3) – d; 4) – d; 5) – a; 6) – a; 7) – a; 8) – d; 9) – b; 10) – d.

TASKS FOR SELF-CONTROL

1. A 36-year-old female patient complains of weight loss, insomnia, unpleasant sensations in the heart area, palpitations. Heart rate 108 per minute. Objectively: the body weight is significantly reduced. A node is palpated on the left half of the neck in the area of the thyroid cartilage. The most possible cause of the heart changes in this case:

a. Excessive secretion of thyroid hormones;
b. Essential tachycardia syndrome;
c. Myocardial diastolic dysfunction;
d. Infectious-inflammatory lesion of the myocardium.

2. A 47-year-old female patient complains of fatigue, increased neck size, weakness, swelling of the face in the morning. She has been sick for 3 years. Objectively: height – 160 cm, weight – 94 kg, pasty face, dry skin, thinning hair, heart rate – 60 bpm. per minute, blood pressure – 100/60 mm Hg. The thyroid gland is enlarged, dense, mobile, painless. What medicines are needed?

a. Mercazolil;
b. L-thyroxine;
c. Hypothiazide;
d. Prednisone

3. A 38-year-old man underwent surgery for DTG. After the operation, the fasting glucose level of whole capillary blood was 4.3 mmol/l, the level of thyroid hormones was normal. 2 months after the operation, an increase in body weight of about 10 kg. Upon re-examination, the glucose level was 5.1 mmol/l, the glycosylated hemoglobin level was 5.1 %, TSH was 12.3 mU/l, FT4 was 7.1 mU/l. What disease can you suspect:

a. Metabolic syndrome;
b. Relapse of diffuse toxic goiter;
c. Glucose intolerance;
d. Postoperative hypothyroidism.

4. A 55-year-old woman with second-degree obesity complains of sudden general weakness, swelling of the face in the morning. Objectively: the skin is pale with a waxy shade, swelling on the hands and feet, pasty face. Laboratory examination revealed hypochromic anemia, increased erythrocyte sedimentation rate, lymphocytosis, and a decrease in T3 and T4 levels in the blood. What is the effective method of treatment in this case:

a. Levothyroxine therapy;
b. Vitamin B12 therapy;
c. Diuretics;
d. Thyrostatics.

5. Female patient M., 38 years old, complains of shortness of breath while walking, palpitations, swelling of the limbs in the evening. Height – 169 cm, body weight – 45 kg. Objectively: the patient is cachectic. Heart tones are weakened, tachycardia up to 140 beats per minute The menstrual cycle is not regular, blood glucose is 4.6 mmol/l. No pathology was detected on the X-ray of the Turkish saddle. During ultrasound examination of the thyroid gland, a diffuse enlargement of the thyroid gland was detected, neoplasms were not visualized. What disease should you think about?

a. Menopause;
b. Hypothyroidism;
c. Hyperthyroidism;
d. Diabetes mellitus.

Keys: 1) – a; 2) – b; 3) – d; 4) – a; 5) – c.

RECOMMENDED LITERATURE

1. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis / Douglas S. Ross, Henry B. Burch, David S. Cooper et al. // Thyroid. – 2016. Vol. 26, No. 10. – P. 1343–1421.http://doi.org/10.1089/thy.2016.0229
2. 5 Lamartina L, Durante C, Lucisano G, Grani G, Bellantone R, Lombardi CP, Pontecorvi A, Arvat E, Felicetti F, Zatelli MC, et al. Are evidence-based guidelines reflected in clinical practice? An analysis of prospectively collected data of the Italian thyroid cancer observatory. *T*hyroid: Official Journal of the American Thyroid Association 2017. 27. P – 1490–1497. (https://doi.org/10.1089/thy.2017.0299)
3. Ali SZ, Baloch ZW, Cochand-Priollet B, Schmitt FC, Vielh P & VanderLaan PA. The 2023 Bethesda system for reporting thyroid cytopathology. Thyroid 2023 [epub]. (https://doi.org/10.1089/ thy.2023. 0141)
4. Angell TE, Maurer R, Wang Z, Kim MI, Alexander CA, Barletta JA, Benson CB, Cibas ES, Cho NL, Doherty GM, et al. A cohort analysis of clinical and ultrasound variables predicting cancer risk in 20,001 consecutive thyroid nodules. Journal of Clinical Endocrinology and Metabolism 2019 104 5665–5672. (https://doi.org/10.1210/jc.2019- 00664)
5. C. Durante**,***, L. Hegedüs**,***, A. Czarniecka et al. 2023 European Thyroid Association Clinical Practice Guidelines for thyroid nodule management. European Thyroid journal. Practice Guideline, Eur Thyroid J. 2023 Aug 14; 12(5):e230067.doi: 10.1530/ETJ-23-0067. Print 2023 Oct 1.
6. Endocrinology and metabolism /Ed. by Pinchera. – London: McGraw Hill Int., 2016. P – 811 p.
7. Grani G, Sponziello M, Pecce V, Ramundo V & Durante C. Contemporary thyroid nodule evaluation and management. Journal of Clinical

Endocrinology and Metabolism 2020. 105. P. – 2869–2883. (https://doi.org/10.1210/clinem/dgaa322)

8. 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, 2014. – 750 p. 28
9. Harrison's Principles of Internal Medicine, 19th edition // DL Kasper, AS Fauci, S L. Hauser et al. – 2015. – P. 2283–2308.
10. Ioakim S, Syed AA, Zavros G, Picolos M, Persani L & Kyriacou A. Real-world application of ATA Guidelines in over 600 aspirated thyroid nodules: Is it time to change the size cut-offs for FNA? European Thyroid Journal 2022, 11, 11.e220163. (https://doi.org/10.1530/ETJ-22-0163)
11. Mario Skodur, Jesse B. Wilder. Thyroid Disorders. – Cleveland Clinic Press, 2016. – 224p.
12. Mu L, Ren C, Xu J, Guo C, Huang J & Ding K. Total versus near-total thyroidectomy in Graves' disease: a systematic review and meta-analysis of comparative studies. Gland Surgery 2021. 10. P – 729–738. (https://doi.org/10.21037/gs-20-757)
13. Russ G, Trimboli P & Buffet C. The New Era of TIRADSs to stratify the risk of malignancy of thyroid nodules: strengths, weaknesses and pitfalls. Cancers 2021 13 4316. (https://doi.org/10.3390/ cancers13174316)

Електронне навчальне видання комбінованого використання
Можна використовувати в локальному та мережному режимі

Тихонова Тетяна Михайлівна
Горшунська Мар'яна Юріївна
Барабаш Надія Євгенівна
Василенко Ольга Олександрівна

ВЕДЕННЯ ПАЦІЄНТА З СИНДРОМОМ ЗОБУ

Методичні рекомендації для підготовки
здобувачів вищої освіти 6-го року навчання
з дисципліни «Внутрішня медицина»

(Англ. мовою)

В авторській редакції

Підписано до розміщення 16.04.2024. Гарнітура Times New Roman.
Ум. друк. арк. 2,67. Обсяг 0,457 Мб. Зам. № 106/24.

Харківський національний університет імені В. Н. Каразіна,
61022, м. Харків, майдан Свободи, 4.
Свідоцтво суб'єкта видавничої справи ДК № 3367 від 13.01.2009

Видавництво ХНУ імені В. Н. Каразіна