DISEASES OF ENDOCRINE SYSTEM
«THE DISEASES OF THYROID GLAND CAUSED BY IODINE DEFICIENCY. CLINICAL PRESENTATION, DIAGNNOSIS, PREVENTION AND TREATMENT. THYROTOXICOSIS. CLINICAL FORMS, DIAGNOSIS, TREATMENT. TUMORS OF THYROID GLAND AND PATHOLOGY OF PARATHYROID GLANDS.»

Methodological recommendations
for students of IV course

ЗАХВОРЮВАННЯ ЕНДОКРИННОЇ СИСТЕМИ.
«ЗАХВОРЮВАННЯ ЩИТОПОДІБНОЇ ЗАЛОЗИ ВНАСЛІДОК ДЕФІЦИТУ ЙОДУ. КЛІНІКА, ДІАГНОСТІКА, ПРОФІЛАКТИКА ТА ЛІКУВАННЯ. ТИРЕОТОКСИКОЗ. КЛІНІЧНІ ФОРМИ, ДІАГНОСТИКА, ЛІКУВАННЯ. ПУХЛИНИ ЩИТОПОДІБНОЇ ЗАЛОЗИ ТА ПАТОЛОГІЯ ПАРАЩИТОПОДІБНИХ ЗАЛОЗ.»

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 -"The diseases of thyroid gland caused by iodine deficiency. Clinical presentation, diagnosis, prevention and treatment. Thyrotoxicosis. Clinical forms, diagnosis, treatment. Tumors of thyroid gland and pathology of parathyroid glands. "

Topicality: Through the hormones it produces, the thyroid gland influences almost all of the metabolic processes in human body. Thyroid disorders can range from a small, harmless goiter that needs no treatment to life-threatening cancer. The most common thyroid problems involve abnormal production of thyroid hormones. Although the effects can be unpleasant or uncomfortable, most thyroid problems can be managed well if properly diagnosed and treated.

The purpose:

1. To determine the etiologic factors and pathogenesis of diffuse toxic goiter. To practice palpation of the thyroid gland.
2. To aquaint students with the classification of goiter after WHO (1992).
3. To learn the typical clinical presentation of diffuse toxic goiter (DTG).
4. To acquaint students with the atypical clinical variants of DTG.
5. To acquaint students with the possible complications of DTG.
6. To determine the basic diagnostic criteria for Graves' disease
7. To make a plan of examination of patients with Graves' disease.
8. To analyze the results of laboratory and instrumental studies, which are used for the diagnosis of DTG.
9. Differential diagnosis between DTG and goiter.
10. The main principles of sustantiation and formulation of the diagnosis of DTG and goiter.
11. To make a treatment plan for patients with DTG and goiter.
12. Deontological and psychological characteristics of supervision of patients with DTG and goiter.

What a student should know?
1. Definition of DTG, goiter, hyperthyroidism.
2. Epidemiology of DTG and goiter in the world.
3. Risk factors for DTG and goiter.
4. The mechanism of hormonal and metabolic disorders in DTG and goiter.
5. Etiology and pathogenesis of DTG and goiter.

6. Classification of degree of thyroid enlargement.
7. The clinical presentation of DTG.
8. The typical clinical presentation of thyrotoxicosis.
9. Multiple organ complications in thyrotoxicosis.
10. Diagnostic criteria of DTG and goiter.
11. Analysis of hormonal tests data.
12. Diagnostic value of the thyroid gland ultrasonography. Radioisotope examination of thyroid gland (radiometry, scanning).
13. Diagnosis of eye lesions and choice of treatment modalities of ocular complications.
14. Selection of treatment for DTG and goiter.

What a student should be able to do?
1. To determine the risk factors for DTG and goiter.
2. To diagnose DTG and goiter.
3. To perform palpation of thyroid gland.
4. To determine the degree of thyroid enlargement.
5. To diagnose the syndrome of thyrotoxicosis.
6. To determine the severity of syndrome of thyrotoxicosis.
7. To detect the presence and nature of ocular complications of DTG.
8. To determine the nature of multiple organ complications in DTG and goiter.
9. To analyze the results of hormonal tests and functional tests.
10. To evaluate the results of ultrasonography and radioisotope examination of thyroid gland.
11. To perform the differential diagnosis between thyrotoxicosis syndrome and goiter.
12. To evaluate the dynamics of thyroid status of patients during thyrostatic treatment.
13. To be able to correct the dose of thyrostatics and accompanying medications as patients achieve euthyroid state.
14. Making of long-term treatment plan for DTG and its complications, patient's engagement in the treatment process.
15. Interaction with related specialists (surgeon, ophthalmologist, cardiologist) during making of complete diagnosis, choice of methods and tactics of treatment and follow-up of patient with Graves' disease or goiter.

Content of the topic
Definition of iodine deficiency. Manifestations of iodine deficiency.

Local symptoms are associated directly with a goiter. Typical complaints are the following: feeling of pressure in the neck, sudden attack of coughing because of the stimulation of recurrent nerve.

Dizziness and headaches are caused by compression of large vessels in the neck area. Because of compression of large vessels a swelling of the face might occur.

Circulatory disturbance extends to the pulmonary circulation and leads to hypertrophy and dilatation of the right ventricle, and so-called «goitre heart» develops.

As a result of the pressure of goiter on the trachea the breath rate rises, also asthma attacks may occur. Sometimes there is discomfort during swallowing as a result of compression of the esophagus. A number of vegetative disorders associated with stimulation or inhibition of the sympathetic nerve trunk and other nerve structures might develop.

With the development of hypothyroidism that accompanies expressed endemic goiter, there is a characteristic clinical picture. Hyperthyroid form of the disease usually runs more mild than the primary thyrotoxicosis. As a result of endemic goiter in few generations an endemic cretinism appears.

Determination of iodine deficiency areas according to the prevalence of goiter in different age groups and according to urinary iodine.

Iodine deficiency leads to insufficient production of thyroid hormones to reduce their secretion. Of feedback reduction of thyroxine in the blood causes a stimulation of the synthesis tyrotropinu. This stimulation is carried out both humoral and neuro-reflex in the form of pulses of the receptor nerve endings in the thyroid gland. Increase tyrotropinu is compensatory hyperplasia of thyroid tissue, thereby increasing hormonopoeza in the thyroid gland and to ensure a sufficient level of thyroxine. In the development of compensatory reactions involved not only tyrotropin but hypothalamic releasing hormone tyroliberyn. In some cases, the process is limited to the initial compensatory hyperplasia of the thyroid gland, which fills the deficiency of thyroid hormones in exogenous iodine deficiency. Another compensatory mechanism is to increase the synthesis of triiodothyronine, which has a higher hormonal activity.

Endemic goiter is common in some mountainous and lowland areas of Ukraine (Carpathians). The prevalence of endemic goiter is determined by several factors: 1) the ratio of men and women with goiter (an indicator of Lenz-Bauer, the more it is closer to unity, the harder it is endemic), 2) the prevalence of nodular goiter forms of its other forms, and

3) the presence of cretinism 4) goiter in animals, and 5) the number of individuals with thyroid hyperplasia.

Iodine deficiency leads to insufficient production of thyroid hormones and decrease of their secretion. According to the feedback principle the reduce of thyroxine level in the blood causes the stimulation of thyrotropin. This stimulation is carried both by humoral and neuro-reflexive ways in the form of impulses from the receptors of nerve endings in the thyroid gland. Increased level of thyrotropin causes compensatory hyperplasia in thyroid tissue, which helps improve hormonopoesis in thyroid gland and ensures adequate level of thyroxine.

Not only thyrotropin is involved into the development of compensatory reaction, but also hypothalamic releasing hormone - thyroliberin. In some cases the process is limited by compensatory hyperplasia of the thyroid gland, which fills the deficiency of thyroid hormones in conditions of exogenous iodine deficiency. Another compensatory mechanism is increasing of synthesis of triiodothyronine, which has a greater hormonal activity.

Endemic goiter is common for the mountaneous and some plains regions in many countries of the world. Prevalence of endemic goiter is determined by a number of indicators: 1) the correlation of men and women with goiter (an indicator of the Lenz-Bauer, the closer it is to 1, the more severe is endemicity), 2) the prevalence of nodular forms of goiter 3) the presence of cretinism; 4) animals with goiter, 5) the number of people with thyroid hyperplasia.

Endemicity is considered as severe if the prevalence of goiter in the population is above 60%, the index of the Lenz-Bauer is 1/3-1/1, the frequency of nodular goiter is higher than 15%, and there are cases of cretinism.

In mild endemicity prevalence of goiter in the population is above 10%, the index of the Lenz-Bauer is 1 / 6, the nodal forms are found in 5% of cases.

Indicators of iodine metabolism

Butanol extractable iodine (BEI) in the blood is made up of a small amount of thyroxine and triiodothyronine. Iodine bound to proteins (IBP) in the blood is made up of thyroxine (90-95%) and mono-and diiodthyronine.

Indicators of IBP more than 670 nmol / L and BEI above 440 nmol / L indicate the hyperfunction of the thyroid gland.

These two methods are very time-consuming, especially the BEI determination, and often demonstrate low accuracy. Investigation of absorption of labeled triiodthyronine by erythrocytes is indicated for

patients who did not receive antithyroid therapy, normally is equal to 11%, and increases depending on the severity of the disease.

Research is uninformative in case of consumption of iodine-containing drugs or concomitant decrease of plasma proteins, reducing of thyroglobulin level.

Iodine prophylaxis: mass, group, individual. The value of consumption of iodized salt in the prevention of iodine deficiency disorders. Limitations in the use of products based on potassium iodide.

The most convenient method of mass iodine prophylaxis is the use of iodized salt. It contains 25 g of potassium iodide in 1 ton of salt. Together with iodine prophylaxis a sea fish and other seafood should be supplied for endemic areas.

Group iodine prophylaxis is done by potassium iodide (1 tablet contains 0.001 g of potassium iodide) in organized groups of children, pregnant and lactating women who have the increased need in thyroid hormones.

Individual iodine prophylaxis is done in persons who had surgery for endemic goiter and to persons living in areas of endemic goiter.

Determination of size of thyroid gland.

Thyroid gland normaly is invisible and is not defined during palpation. During palpation we are looking for the thyroid gland in the front of the neck, near the lower edge of thyroid cartilage on either sides of it. The thyroid gland gives the impression of roller, which rolls during the swallowing movements.

On the view we should pay attention to the shape of the neck, the presence of pulsations and outpouching of thyroid gland. Most thyroid diseases are accompanied by increasing of thyroid gland, but absence of increased thyroid gland does not exclude the presence of pathology. The thyroid gland may be enlarged diffusely or through its individual parts.

During palpation pay attention not only on quantity, but also at the location of the thyroid gland and its texture (elastic, dense, soft, and woody). Assess the nature of the surface of the thyroid gland (smooth, bumpy), mobility, presence of pain during palpation. Thyroid enlargement is observed in diffuse toxic goiter, sporadic and endemic goiter, inflammatory diseases, and cancer.

Definition of "goiter"

The clinical term *"nodular goiter"* combines focal thyroid lesions, which have different pathomorphological structure - the cysts, nodes, benign and malignant tumors of the thyroid gland. Tumors of

the thyroid gland in most cases are of epithelial origin - an adenoma and adenocarcinoma.

Endemic goiter – is a disease that occurs in certain biogeochemical geographic areas with iodine deficiency in the environment, and is characterized by enlargement of the thyroid gland.

Sporadic goiter is persistent increase of thyroid gland among residents of areas without iodine deficiency (a physiological providing of iodine).

Goiter is an enlargement of the thyroid gland of third degree or higher. The increase of thyroid gland of 2nd degree is called thyroid hyperplasia, but in the presence of node this variant is also called goiter.

WHO classification of endemic goiter:

Group 0. No goiter.

Group 1. Goiter is determined by palpation. The thyroid gland is clearly visible when head is turned back and neck is elongated.

Group 2. Goiter is determined visually.

Group 3. Goiter is seen at a distance, grows up to large sizes, mechanicaly makes breathing difficult.

By the form of increased thyroid gland, the presence or absence of nodes:

- Nodular goiter (characterized by tumorlike growth of thyroid tissue, often is round in shape, mainly it has elastic consistency, other sections of thyroid gland usually are not palpable);

- Diffuse goiter (characterized by an even increase of the thyroid gland in the absence of local consolidations);

- Mixed, or diffuse nodular goiter (union of the diffuse hyperplasia and node).

Diseases that are accompanied by thyrotoxicosis.

Thyrotoxicosis (hyperthyroidism) – is a syndrome, whose presence is associated with an increased content of thyroid hormones in the blood, which occurs with various diseases or excessive exogenous entry of thyroid hormones.

Thyrotoxicosis is observed in diffuse toxic goiter, multinodular toxic goiter, thyrotoxic adenoma, subacute thyroiditis (first 1-2 weeks), postpartum (silent) thyroiditis, autoimmune thyroiditis, thyroiditis that developed after exposure to ionizing radiation, syndrome of not adjustable

TSH secretion, follicular thyroid cancer and its metastases, ectopic goiter (ovarian tissue), excessive intake of iodine (iodine-hyperthyroidism), trophoblastic tumors, which secrete human chorionic gonadotropin, iatrogenic and "artificial or conditional" thyrotoxicosis.

The etiology, pathogenesis, clinical manifestations of diffuse toxic goiter.

Diffuse toxic goiter - thyroid disease, which manifests with diffuse thyroid enlargement and thyrotoxicosis. The disease has many names - the names of authors who had described it - Basedow's disease (in Germany), Grave's disease (in Britain), and Flajani`s disease (in Italy), "hyperthyroidism with diffuse thyroid enlargement", "autoimmune thyrotoxicosis".

The disease is more common in women than in men (correlation is 5:1, 7:1), and affects mainly those aged 30-50 years.

Diffuse toxic goiter - autoimmune disease that develops in patients with heredity. The nature of inheritance is still being discussed– autosomal recessive or autosomal dominant. The most probable is multifactorial (polygenic) inheritance type.

It is determined, that during diffuse toxic goiter the suppressor activity of mononuclear cells in peripheral blood is significantly reduced, and this immune defect persists even after these patients achieve euthyroid state as a result of thyreostatic treatment. Reduced activity of T suppressors is specific congenital disorder in individuals predisposed to the development of diffuse toxic goiter.

Clinical manifestations

In most cases, the development of diffuse toxic goiter occurs slowly, symptoms increase gradually. The disease progresses. However, there are some cases of acute disease development.

1. The lesion of the thyroid gland

Goiter is enlarged thyroid gland of various degrees, this is a characteristic feature of diffuse toxic goiter.

The thyroid gland is uniformly, diffusely enlarged, palpated on the anterior and lateral surfaces of the neck. In most cases the gland is increased to II-III degree. The degree of increased thyroid gland often does not correspond to the severity of the disease. The size of goiter can vary: it increases after excitement, after initiation of treatment it is gradually reduced.

As a rule, men with severe clinical form of diffuse toxic goiter have the thyroid gland increased slightly, palpated with difficulty, since gland is increased mainly by lateral lobes, which lie close to the trachea.

Gland is not palpable when it is located in atypical position - the ring-like (gland is located as a ring around the trachea) and retrosternal goiter.

There are several classifications of the degrees of thyroid enlargement. One of the is clinical classification proposed by O.V. Nikolaev in 1955.

0 degree - the thyroid gland is not palpable;

I degree - the increase of isthmus of thyroid gland is determined by palpation;

II degree - the increase of the lateral lobes of thyroid gland;

III degree - the increase of thyroid gland can be visually determined ("bull neck");

IV degree - a significant increase of thyroid gland (goiter clearly visible);

V degree - huge goiter.

I and II degrees are attributed to the increase of thyroid gland, and the III-V degrees of increased thyroid gland is actually goiter.

Also WHO classification is used (1992):

0 degree - goiter is not visible and not palpable;

I degree - the formation is palpated on the neck corresponding to the enlargement of the thyroid gland, is shifted during swallowing, but not visible in normal neck position, one or more nodes can be palpated in the thyroid gland;

II degree – thyroid gland is palpable and clearly visible in the normal position of the head.

2. The impairment of the cardiovascular system

Cardiovascular disorders occupy the dominate place in the clinical picture of thyrotoxicosis.

Cardiovascular disorders in diffuse toxic goiter are caused, on the one hand, by the pathological sensitivity of the cardiovascular system to catecholamines, on the other hand - by direct impact of the excess of thyroxine on the myocardium. The disorder of hemodynamics, the disparity between the level of delivery, consumption and utilization of oxygen to the heart muscle leads to severe metabolic-dystrophic damage and the development of thyrotoxic cardiomyopathy.

A. Stage of functional disorders.

At the stage of functional disorders the symptoms are caused by hypercatecholemia, hypersensitivity of receptors, hypersympathicotonia. The hyperkinetic type of hemodynamics with increasing of the cardiac performance, increased blood flow is formed.

Palpitations are typical, which increase during exercise.

Tachycardia is constant, it does not change with a change of body position from vertical to horizontal, and does not disappear during sleep. Frequency of heart rate ranges from 90 to 150 beats per minute, extrasystole is possible.

Specific for thyrotoxicosis is the opposite changes in systolic blood pressure (increase) and diastolic blood pressure (reduction). Systolic blood pressure is high caused by the hyperkinetic type of circulation with increased heart stroke volume and cardiac output.

The multidirectional changes of blood pressure are specific to thyrotoxicosis: increased systolic and decreased diastolic blood pressure. Systolic blood pressure increases as a result of hyperkinetic type of circulation with increased cardiac stroke volume and cardiac output.

Diastolic pressure is reduced by reducing the total peripheral vascular resistance caused by the expansion of peripheral arterioles. Paresis of peripheral vessels is a factor of adaptation - an increase in blood vessels of the skin improves heat transfer and prevents "overheating" of internal organs (and also provides short-term anti-aging dermatological effect of short-term hyperthyroidism). Skin is warm to the touch, moist due to compensatory expansion of peripheral blood vessels.The difference between systolic and diastolic blood pressure (pulse pressure) increases significantly, and causes a subjective sensation of pulsation of the neck vessels, feeling of the pulse in the neck, head and abdomen.

Pulse is accelerated, has increased content and stress.

There is nagging pain in the heart (cardialgia) or angina - usually in patients with concomitant coronary artery disease.

Heart sounds are loud, a functional systolic murmur with a peak at Botkin`s point, at the basis of the heart, blood vessels in the neck is auscultated. The origin of the murmur is associated with the acceleration of blood flow, widening of pulmonary artery, swelling of the papillary muscles. In the early stages of development of toxic goiter the borders of the heart are not changed.

The ECG - tachycardia, high voltage of P and T waves.

The dyspnea, palpitations, intermissions are caused by the addition of circulatory deficiency.

Severe cardiac arrhythmias are typical - eusystole, tachysistole form of ciliary arrhythmia, paroxysmal or permanent form.

The ciliary arrhythmia has a paroxysmal character at the beginning, and then goes into the persistent form. The ciliary arrhythmia may be associated with extrasystole. Paroxysms of the ciliary arrhythmia sometimes can be the only manifestation of diffuse toxic goiter. Abnormal heart rate often occurs in patients older than 40 years.

Permanent form of the ciliary arrhythmia leads to the progression of circulatory failure by right ventricular type with an increase of the liver, peripheral edema, extravasation into the pleural cavity, ascites.

Circulatory failure and arrhythmias in case of thyrotoxic cardiomyopathy are resistant to cardiac glycosides.

In the elderly age thyrotoxicosis may manifest itself by attack of the ciliary arrhythmia, which creates a difficulty for the diagnosis of the disease. In the normal periods patient's general condition remains satisfactory, and heart rate may be within normal limits.

The expansion of the heart is caused by the overload of myocardium (the symptom of Grokko).

The ECG: sinus tachycardia, sinus arrhythmia, atrial flutter, atrial or ventricular extrasystoles, ciliary arrhythmia, acceleration or deceleration of atrioventricular conduction.

Signs of hypoxia and focal ischemia of the left ventricle: the derangements of the ultimate part of ventricular complex (depression of ST segment, negative or biphasic T wave). Signs of myocardial "fatigue" - the amplitude and duration of P and T waves are reduced.

3. Psycho-emotional disorders

Disorders of the nervous and psychic activity are the important manifestations of diffuse toxic goiter.

Diffuse toxic goiter is characterized by irritability, excitability, and lability of mood. These patients are excessively active, restless, fidgety, conflict, mistrust, intolerant, unable to concentrate. Working ability and memory are reduced.

4. Thyrotoxic encephalopathy

The lesion of central nervous system can develop as thyrotoxic encephalopathy. In this case, patients have such complains as headache, dizziness, photophobia, disturbance of sleep.

Sometimes autoimmune encephalitis is revealed. The damage of brain in the region of stem and hypothalamus is possible, usually caused by leukocyte infiltration, degeneration of cells in the brain stem and the hypothalamus nuclei, medulla oblongata.

The patients also have clinical signs of pyramidal tract lesions: hyperreflexia, anizorefleksiya, the absence of cutaneous reflexes, the presence of reflexes of oral automatism, central paresis of mimic muscles, disorders of coordination.

The central paresis of facial muscles, pyramidal signs (hyperreflexia, anizoreflexia), paresis and muscle atrophy are sometimes determined.

5. Thyrotoxic myopathy

One of the early and persistent symptoms of the disease is muscular weakness. It varies from a sense of expressed fatigability to severe muscle weakness and atrophy of muscles of the proximal extremities. The most expressed is the lesion of muscles of the pelvic girdle and thighs, rare the shoulder girdle and hands.

Patients can not stand up without assistance, walk up the stairs.

6. Thyrotoxic myelopathy

Thyrotoxic myelopathy is the involvement of the anterior horns of the spinal cord, manifested by muscle atrophy and paresis of the proximal parts of extremities, mainly the pelvic girdle. Thyrotoxic myelopathy is combined with thyrotoxic myopathy in severe cases.

7. Dysfunction of the gastrointestinal tract

The most frequent symptom of diffuse toxic goiter - a progressive weight loss with increased appetite. In the elderly age the appetite may be reduced.

"Fat Bazedov" is possible - growth of weight during thyrotoxicosis, especially in men.

Evident thyrotoxicosis is accompanied by an increase of intestinal peristalsis – the frequentcy of stool is up to 3-4 times a day, with a formed or semi-liquid feces. During severe thyrotoxicosis patients can have frequent diarrhea, which exhausts the patient. Sometimes spastic constipation is developed.

Thyrotoxic and endocrine ophthalmopathy.

A. Ocular symptoms of thyrotoxicosis

Most of patients have protrusion of the eyeballs - exophthalmus.

Thyrotoxic exophthalmus is a functional disorder caused by hypercatecholemia and disorders of the vegetative innervation of the eye.

Thyrotoxic exophthalmus usually develops with the manifestation of the disease, usually develops gradually, but sometimes within a few days or even hours. In some cases it is the first symptom of thyrotoxicosis.

As a rule, exophthalmos is bilateral, symmetric, and rarely unilateral.

There is no disturbance of eye function; there is no double vision.

There is no parallelism between the severity of diffuse toxic goiter and exophthalmus degree. Thyrotoxic exophthalmus completely disappears after compensation of thyrotoxicosis.

Symptoms related to abnormality of oculomotor responses:

Wilder - a twitch of the eyeball during alternate reduction and abduction.

Mobius - during a fixed view on a close subject eyes can not be in a position of convergence for long period of time, and then one of them soon moves outwards.

Cowan – during checking of simultaneous reaction of pupils the pupillar vibration is observed.

Development of the following symptoms is associated with an increased tone of smooth muscle fibers, which are involved in the lifting of the upper eyelids, which are innervated by the sympathetic nervous system.

When patient gazes fixation on an object that moves in front of his eyes down, the following symptoms are observed:

1. *Graefe's* - upper eyelid initially lags behind and then catches up with iris eyeball that moves, and thus appears white stripe between the upper eyelids, sclera and iris.

2. *Popov's* - upper eyelid patient falls abruptly.

3. *Senton's* – patient's upper eyelid elevates through a spastic contraction of frontal muscle.

When patient gazes fixation on an object that moves in front of his eyes upward, the following symptoms are observed:

Kocher's - upper eyelid moves up faster than the eyeball with a white strip of sclera between the upper eyelid and iris.

B. Autoimmune ophthalmopathy

Autoimmune ophthalmopathy is an independent autoimmune disease. It is the immunocomplex lesion of orbit tissues accompanied by infiltration, edema and proliferation of postbulbar muscle fibers and connective tissue. Synonyms of autoimmune ophthalmopathy, previously used in clinical practice: edematous exophthalmus, malignant

exophthalmus, exophthalmus neurodystrophic, orbitopathy, endocrine exophthalmus.

Autoimmune ophthalmopathy can occur as a separate disease, independent from thyrotoxicosis, or combined with diffuse toxic goiter or local myxedema.

Characteristic symptoms of autoimmune ophthalmopathy: exophthalmus, conjunctivitis and keratitis.

Exophthalmus in autoimmune ophthalmopathy is asymmetric, may be unilateral, is combined with edema and infiltration of the eyelids.

Constant symptom is double vision (diplopia) caused by changes in the oculomotor muscles.

Normally, the protrusion of the eyeball is 16-19 mm. There are three degrees of ophthalmopathy during which protrusion of the eyeball increases till 3-4 mm, 5-7 mm and above 8 mm.

Conjunctivitis that is complicating ophthalmopathy, manifests by lacrimation, photophobia, burning of eyes, feeling of foreign body, "sand" in the eyes, feeling of pressure on eyes, pain in eyeballs. There is typically hyperemia, edema of the conjunctiva, eyelid edema, injection of scleral vessels, restricted movements of the eyeball, reduced corneal reflexes. Neoplasm of vessels is a bad prognostic sign.

Keratitis develops during a significant ophthalmopathy (III degree) - eyeballs protrude from the orbit, eyelids and conjunctiva are swollen, inflamed; inflammation and ulceration are formed because of permanent drying of the cornea, that can lead to corneal leukoma and the reduction of vision up to complete blindness.

Diagnosis of thyrotoxicosis.
- TSH
- Free T_4, plus either free T_3 or total T_3
- Radioactive iodine uptake

Diagnosis is based on history, physical examination, and thyroid function tests. Serum TSH measurement is the best test because TSH is suppressed in hyperthyroid patients except in the rare instance when the etiology is a TSH-secreting pituitary adenoma or pituitary resistance to the normal inhibition by thyroid hormone. Screening selected populations for TSH level is warranted. Free T_4 is increased in hyperthyroidism. However, T_4 can be falsely normal in true hyperthyroidism in patients with a severe systemic illness (similar to the falsely low levels that occur in euthyroid sick syndrome) and in T_3 toxicosis. If free T_4 level is normal and TSH is low in a patient with subtle symptoms and signs of hyperthyroidism, then serum

T_3 should be measured to detect T_3 toxicosis; an elevated level confirms that diagnosis.

The cause can often be diagnosed clinically (exposure to a drug, the presence of signs specific to Graves' disease). If not, thyroid radioactive iodine uptake may be obtained by using [123]I. When hyperthyroidism is due to hormone overproduction, thyroid radioactive iodine uptake is usually elevated. When hyperthyroidism is due to thyroiditis, iodine ingestion, or ectopic hormone production, radioactive iodine uptake is low.

TSH receptor antibodies can be measured to detect Graves' disease, but measurement is rarely necessary except during the 3rd trimester of pregnancy to assess the risk of neonatal Graves' disease; TSH receptor antibodies readily cross the placenta to stimulate the fetal thyroid. Most patients with Graves' disease have circulating antithyroid peroxidase antibodies, and fewer have antithyroglobulin antibodies.

Inappropriate TSH secretion is uncommon. The diagnosis is confirmed when hyperthyroidism occurs with elevated circulating free T_4 and T_3 concentrations and normal or elevated serum TSH.

If thyrotoxicosis factitia is suspected, serum thyroglobulin can be measured; it is usually low or low-normal—unlike in all other causes of hyperthyroidism.

TREATMENT
Medical treatment:

Methimazole and Propylthiouracil: These antithyroid drugs block thyroid peroxidase, decreasing the organification of iodide, and impair the coupling reaction. Propylthiouracil in high doses also inhibits the peripheral conversion of T_4 to T_3. About 20 to 50% of patients with Graves' disease remain in remission after a 1- to 2-yr course of either drug. The return to normal or a marked decrease in gland size, the restoration of a normal serum TSH level, and less severe hyperthyroidism before therapy are good prognostic signs of long-term remission. The concomitant use of antithyroid drug therapy and L-thyroxine does not improve the remission rate in patients with Graves' disease. Because toxic nodular goiter rarely goes into remission, antithyroid drug therapy is given only in preparation for surgical treatment or ^{131}I therapy.

Because of severe hepatic failure in some patients < 40, especially children, propylthiouracil is now recommended only in special situations (in the 1st trimester of pregnancy, in thyroid storm).Methimazole is the preferred drug. The usual starting dosage of methimazole is 5 to 20 mg po tid and of propylthiouracil 100 to 150 mg per os every 8 h. When T_4 and T_3 levels normalize, the dosage is decreased to the lowest effective amount,

usually methimazole 5 to 15 mg once/day or propylthiouracil 50 mg 3/day. Usually, control is achieved in 2 to 3 months. More rapid control can be achieved by increasing the dosage ofpropylthiouracil to 150 to 200 mg every 8 h. Such dosages or higher ones (up to 400 mg every 8 h) are generally reserved for severely ill patients, including those with thyroid storm, to block the conversion of T_4 to T_3. Maintenance doses of methimazole can be continued for one or many years depending on the clinical circumstances. Carbimazole, which is used widely in Europe, is rapidly converted to methimazole. The usual starting dose is similar to that of methimazole; maintenance dosage is 5 to 20 mg per os once/day, 2.5 to 10 mg 2/day, or 1.7 to 6.7 mg 3/day. Adverse effects include rash, allergic reactions, abnormal liver function (including hepatic failure with propylthiouracil), and, in about 0.1% of patients, reversible agranulocytosis. Patients allergic to one drug can be switched to the other, but cross-sensitivity may occur. If agranulocytosis occurs, the patient cannot be switched to the other drug; other therapy (radioiodine, surgery) should be used.

Each drug has advantages and disadvantages. Methimazole need only be given once/day, which improves adherence. Furthermore, when methimazole is used in dosages of < 40 mg/day, agranulocytosis is less common; with propylthiouracil, agranulocytosis may occur at any dosage.Methimazole has been used successfully in pregnant and nursing women without fetal or infant complications, but rarely methimazole has been associated with scalp and GI defects in neonates and with a rare embryopathy. Because of these complications, propylthiouracil is used in the 1st trimester of pregnancy. Propylthiouracil is preferred for the treatment of thyroid storm, because the dosages used (800 to 1200 mg/day) partially block the peripheral conversion of T_4 to T_3. The combination of high-dose propylthiouracil and dexamethasone, also a potent inhibitor of T_4 to T_3conversion, can relieve symptoms of severe hyperthyroidism and restore the serum T_3 level to normal within a week.

β-Blockers: Symptoms and signs of hyperthyroidism due to adrenergic stimulation may respond to β-blockers; propranolol has had the greatest use, but atenolol or metoprolol may be preferable. Other manifestations typically do not respond.

- Manifestations typically responding to β-blockers: Tachycardia, tremor, mental symptoms, eyelid lag; occasionally heat intolerance and sweating, diarrhea, proximal myopathy
- Manifestations typically not responding to β-blockers: O_2 consumption, exophthalmos, goiter, bruit, circulating thyroxine levels, weight loss

Propranolol is indicated in thyroid storm. It rapidly decreases heart rate, usually within 2 to 3 h when given orally and within minutes when given IV. Esmolol may be used in the intensive care unit because it requires careful titration and monitoring. Propranolol is also indicated for tachycardia with hyperthyroidism, especially in elderly patients, because antithyroid drugs usually take several weeks to become fully effective. Ca channel blockers may control tachyarrhythmias in patients in whom β-blockers are contraindicated.

Iodine: Iodine in pharmacologic doses inhibits the release of T_3 and T_4 within hours and inhibits the organification of iodine, a transitory effect lasting from a few days to a week, after which inhibition usually ceases. Iodine is used for emergency management of thyroid storm, for hyperthyroid patients undergoing emergency nonthyroid surgery, and (because it also decreases the vascularity of the thyroid) for preoperative preparation of hyperthyroid patients undergoing subtotal thyroidectomy. Iodine generally is not used for routine treatment of hyperthyroidism. The usual dosage is 2 to 3 drops (100 to 150 mg) of a saturated K iodide solution per os 3/day or 4/day or 0.5 to 1 g Na iodide in 1 L 0.9% saline solution given IV slowly every 12 h.

Complications of iodine therapy include inflammation of the salivary glands, conjunctivitis, and rash.

Surgical treatment

Indications for surgical treatment:

1) The inefficiency of drug therapy for 4-6 months from the beginning of treatment – the exacerbation of the disease at maintaining dose of thyreostatics

2) Rapid enlargement of the thyroid gland till 4-5 degrees;

3) High density of the thyroid gland with symptoms of compression of the neck;

4) Severe thyrotoxicosis;

5) Cancellation of mercasolil due to allergy, granulocytopenia;

6) Recurrent toxic goiter;

7) Thyrotoxicosis complicated by encephalopathy or ophthalmopathy;

8) The development of complications of diffuse toxic goiter in patients with associated diabetes mellitus;

9) The nodal, mixed, atypical, and aberrant forms of goiter;

10) Pregnancy and lactation;

11) Severe thyrotoxicosis complicated by ciliary arrhythmia.

Complications of surgical treatment:

1) Postoperative thyroid storms,

2) The injury or paresis of recurrent nerve;
3) The hypoparathyroidism and tetany;
4) Early hypothyroidism (up to 6 months);
5) Late hypothyroidism (over 6 months after surgery);
6) Recurrence of the disease;
7) Postthyrotoxic encephalopathy

Treatment with radioactive iodine

Therapeutic use of radioactive iodine. Treatment method is based on the property of thyroid gland to absorb radioactive iodine selectively. Beta-rays formed by the decay of radioactive iodine, destroy the cellular elements of the thyroid parenchyma, but they do not destroy surrounding tissue because of a short-range (2 mm) beams. Iodine-131 is used for the treatment. Patients should be over 40 years old.

Indications for radioactive iodine therapy:

1) Patients with severe heart failure in which surgical treatment is risky;

2) A combination of diffuse toxic goiter with tuberculosis, severe hypertension, myocardial infarction, psychiatric disorders, hemorrhagic syndrome;

3) Relapse of thyrotoxicosis after subtotal thyroidectomy;

4) Patient's refusal to undergo surgical treatment.

Contraindications for the radioactive iodine treatment: pregnancy, lactation, young age, a major degree of thyroid enlargement or retrosternal location of goiter, blood diseases, kidney diseases, peptic ulcer, nodular forms of goiter.

Cancer of thyroid gland.

The 4 general types of thyroid cancer are *papillary, follicular, medullary, and anaplastic*. Papillary and follicular carcinoma together are called differentiated thyroid cancer because of their histologic resemblance to normal thyroid tissue and because differentiated function (thyroglobulin secretion) is preserved. Most thyroid cancers manifest as asymptomatic nodules. Rarely, lymph node, lung, or bone metastases cause the presenting symptoms of small thyroid cancers. Diagnosis is often by fine-needle aspiration biopsy but may involve other tests.

PAPILLARY CARCINOMA

Papillary carcinoma accounts for 70 to 80% of all thyroid cancers. The female:male ratio is 3:1. It may be familial in up to 5% of patients. Most patients present between ages 30 and 60. The tumor is often more aggressive in elderly patients. Many papillary carcinomas contain follicular elements.

The tumor spreads via lymphatics to regional lymph nodes in one third of patients and may metastasize to the lungs. Patients < 45 years with small tumors confined to the thyroid have an excellent prognosis.

Treatment

- Surgical resection
- Sometimes radioactive iodine

Treatment for encapsulated tumors < 1.5 cm localized to one lobe is usually near-total thyroidectomy, although some experts recommend only lobectomy and isthmectomy; surgery is almost always curative. Thyroid hormone in thyroid-stimulating hormone (TSH)–suppressive doses is given to minimize chances of regrowth and cause regression of any microscopic remnants of papillary carcinoma.

Tumors > 4 cm or that are diffusely spreading require total or near-total thyroidectomy with postoperative radioiodine ablation of residual thyroid tissue with appropriately large doses of ^{131}I administered when the patient is hypothyroid or after recombinant TSH injections. Treatment may be repeated every 6 to 12 mo to ablate any remaining thyroid tissue. TSH-suppressive doses of L-thyroxine are given after treatment, and serum thyroglobulin levels help detect recurrent or persistent disease. About 20 to 30% of patients, mainly older patients, have recurrent or persistent disease.

FOLLICULAR CARCINOMA

Follicular carcinoma, including the Hurthle cell variant, accounts for about 15% of thyroid cancers. It is more common among older patients and in regions of iodine deficiency. It is more malignant than papillary carcinoma, spreading hematogenously with distant metastases.

Treatment requires near-total thyroidectomy with postoperative radioiodine ablation of residual thyroid tissue as in treatment for papillary carcinoma. Metastases are more responsive to radioiodine therapy than are those of papillary carcinoma. TSH-suppressive doses of L-thyroxine are given after treatment. Serum thyroglobulin should be monitored to detect recurrent or persistent disease.

MEDULLARY CARCINOMA

Medullary (solid) carcinoma constitutes about 3% of thyroid cancers and is composed of parafollicular cells that produce calcitonin. It may be sporadic (usually unilateral); however, it is often familial, caused by a mutation of the *ret* proto-oncogene. The familial form may occur in

isolation or as a component of multiple endocrine neoplasia (MEN) syndromes types 2A and 2B. Although calcitonin can lower serum Ca and phosphate, serum Ca is normal because the high level of calcitonin ultimately down-regulates its receptors. Characteristic amyloid deposits that stain with Congo red are also present.

Metastases spread via the lymphatic system to cervical and mediastinal nodes and sometimes to liver, lungs, and bone.

Symptoms and Signs

Patients typically present with an asymptomatic thyroid nodule, although many cases are now diagnosed during routine screening of affected kindreds with MEN 2A or MEN 2B before a palpable tumor develops.

Medullary carcinoma may have a dramatic biochemical presentation when associated with ectopic production of other hormones or peptides (ACTH, vasoactive intestinal polypeptide, prostaglandins, kallikreins, serotonin).

Diagnosis.

The best test is measurement of *serum calcitonin*, which is greatly elevated. A challenge with Ca (15 mg/kg IV over 4 h) provokes excessive secretion of calcitonin. X-rays may show a dense, homogenous, conglomerate calcification.

All patients with medullary carcinoma should have genetic testing; relatives of those with mutations should have genetic testing and measurement of basal and stimulated calcitonin levels.

Treatment.

Surgical resection: total thyroidectomy is indicated even if bilateral involvement is not obvious. Lymph nodes are also dissected. If hyperparathyroidism is present, removal of hyperplastic or adenomatous parathyroids is required. Pheochromocytoma, if present, is usually bilateral. Pheochromocytomas should be identified and removed before thyroidectomy because of the danger of provoking hypertensive crisis during the operation. Long-term survival is common in patients with medullary carcinoma and MEN 2A; more than two thirds of affected patients are alive at 10 years. Medullary carcinoma of the sporadic type has a worse prognosis.

Relatives with an elevated calcitonin level without a palpable thyroid abnormality should undergo thyroidectomy because there is a greater chance of cure at this stage. Some experts recommend surgery in relatives who have normal basal and stimulated serum calcitonin levels but who have the *ret* proto-oncogene mutation.

ANAPLASTIC CARCINOMA

Anaplastic carcinoma is an undifferentiated cancer that accounts for about 2% of thyroid cancers. It occurs mostly in elderly patients and slightly more often in women. The tumor is characterized by rapid, painful enlargement. Rapid enlargement of the thyroid may also suggest thyroid lymphoma, particularly if found in association with Hashimoto's thyroiditis.

No effective therapy exists, and the disease is generally fatal. About 80% of patients die within 1 year of diagnosis. In a few patients with smaller tumors, thyroidectomy followed by external radiation has been curative. Chemotherapy is mainly experimental.

Diseases of parathyroid glands.
HYPERPARATHYROIDISM.

Hyperparathyroidism is a disease of parathyroid glands which is characterized by increase of secretion of parathormone and development of hypercalcaemia.

Etiology, classification. Primary hyperpathyroidism is more often caused by an adenoma or hyperplasia and less often by a carcinoma of parathyroid glands. Adenomas of parathyroid glands can be single or plural, and appear in 80-85 % of patients. Hyperplasia is observed in 15-20 % of patients. The cancer of parathyroid glands accounts for 0,5-3 % of cases.

Hyperparathyroidism is caused by hyperplasia or new growths of parathyroid glands, can be sporadic or family based, with an autosome-dominant type of inheritance. Hereditary primary hyperparathyroidism is quite often the component of multiple endocrine adenomatosis (MEA) or multiple endocrine neoplasia (MEN). MEN type I can be found in 90 % of patients and MEN type II - in 10-50 % of patients. In both cases hyperparathyroidism is caused by hyperplasia of all parathyroid glands, less often it is caused by adenoma.

Pathogenesis. Development of adenoma of parathyroid glands is caused by two types of mutations. I type is a mutation in mitosis control; II type is a mutation of the mechanism of the final control of parathormone secretion. It is considered, that the mutation affects one of genes which code proteins taking part in transport of calcium into the cells of parathyroid glands.

The mutant cell has increased secretory activity and gives a new clone of cells, their number increases uncontrollably along with formation of an adenoma, which sometimes performes an independent secretion of a hormone. The population of quickly proliferating cells of parathyroid gland might occur in some cases under the influence of calcitriole or low calcium level, which leads either to primary or secondary hyperplasia or to

hyperplastic adenoma, and may also cause the development of polyclonal adenomas of parathyroid glands.

Clinical presentation and clinical forms of hyperparathyroidism.

Primary hyperparathyroidism, caused by hypercalcemia due to parathormone hypersecretion, manifests by great variety of symptoms. Clinical forms: bone, renal, gastrointestinal (peptic ulcer, pancreatitis, cholecystitis), cardiovascular (arterial hypertension) and others.

In 50 % of cases disease is asymptomatic and only hypercalcemia allows suspecting hyperparathyroidism.

Clinical presentation of primary hyperparathyroidism is characterized by the lesion of *central nervous system*: fatigue, weakness, headache, depression, infringement of appetite, psychoses and comas.

Lesion of muscles and joints: myopathy, gout, pseudogout, chondrocalcinoses, erosive arthritis.

Lesion of eyes: cataract, calcium deposits in the superficial layers of the cornea.

Cardiovascular system: calcification of the heart and blood vessels, the development of hypertension and arrhythmias.

Lesions of digestive organs: the development of gastro-esophageal reflux disease, gastric ulcer and duodenal ulcer, gallstones, pancreatitis, constipation.

Lesions of kidneys: polyuria and polydypsia, decreased concentration ability of the kidneys, the development of urolithiasis, nephrocalcinosis and renal tubular acidosis.

The clinical presentation may become complicated by the presence of fever and development of anemia.

It should be noted that the atrophic process involves large muscle groups with a decrease in the amplitude of their contraction potentials.

Sometimes there are severe bone lesions with the presence of fibrocystic osteitis and replacement of bone marrow hemopoietic tissue by connective tissue.

Diagnosis of hyperparathyroidism.

The biopsy of a bone tisuue is indicated for confirmation of the diagnosis. Regardless of the severity of the disease, the thinning of bones compact substance is defined histologically, replacement of a bone tissue by fibrous tissue with a plenty of osteoclasts and macrophages, loaded with hemosiderin (cysts and brown tumors).

Densitography of bones shows significant decrease of density of a bone tissue, diffuse demineralisation of a bone tissue, diffuse osteolysis,

subperiostal resorption of a bone tissue in phalanxes of fingers, subperiostal erosions in long tubular bones and bones of a skull.

At percussion of skull bones there is a sound of ''ripe water-melon''. Various degrees of osteoporosis can be seen in the bones of the spine. Such patients also have an increased risk of spontaneous fractures of the forearm bones, femur and spine. Often, patients notice a decrease in body height during illness and changes of body proportions. In a standing position hands can reach the level of the knee joint.

Nephrolithiasis is characterized by presence of one stone or plural calculi in both kidneys. Surgical removal of a stone does not lead to recover. Stones of kidneys consist of oxalate or phosphate of calcium. Nephrocalcinosis occurs rarely. It is characterized by calcifications of renal tubules (epithelial layer, base membranes and interstitial layer), with decrease of glomerule filtrations and functions of proximal departments of renal tubules (aminoaciduria, glycosuria, decrease in concentration ability of kidneys).

The stomach ulcer is characterized by the frequent exacerbations, the marked pain syndrome and quite often becomes complicated by perforation. The dairy diet and alkaline salts as medical means are not recommended, as they lead to development a hypercalcimic crisis (hyperparathyroidism and alkalic-lactic syndrome). The peptic ulcer can be the sign of MEN I or MEN II syndrome, and also can be associated with Zollinger-Ellison syndrome.
Lesion of cardiovascular system is characterized by adjournment of salts of calcium in a myocardium, calcification of coronary arteries and valves of heart (aortic, mitral), a hypertrophy of left ventricle and presence of a hypertension.

Laboratory diagnosis includes a number of tests.

1. Determination of concentration of free calcium in blood serum. Sometimes concentration of free calcium remains normal even if parathormone is increased (normocalcemic hyperparathyroidism), it can be caused by disorders of tubule reabsorption of calcium, calcium absorption in intestines, presence of D avitaminosis (hypercalcemia develops at accompanying treatment with vitamin D, at isolated - restoration of normal calcemia); at early stages of primary hypercalcemia. The reliability of the diagnosis should be confirmed by provocative test with thiazide diuretics: if hyperparathyroidism is absent it normalizes up to the end of the first week under hydrocotisone treatment.
1. Determination of parathormone level in blood serum along with simultaneous measurement of the common or free calcium.
2. Determination of a level of the common or nephrogenic cAMP in urine.
3. Determination of a level of calcium in urine (can be normal or increased)

4. Determination of phosphates in blood serum (hypophospataemia occurs at lower threshold of tubule reabsorption of phosophate and reduction of the relation in maximal tubule phosphate reabsortion to the velocity of tubule filtration).

5. Determination of the relation of chloride/phosphates in blood serum (normal value - less than 32).

6. Determination of alkaline phosphotase, proteins, creatinine, residual nitrogen of blood serum.

7. CBC (normochromic anemia, moderate leucocutosis and increased ESR).

Instrumental diagnosis:

1. Ultrasound exam in 50-60 % of cases allows revealing increased parathyroid glands.

2. CT and MRI allow revealing the lesion of parathyroid glands in 90 % of cases.

3. Subtractional scintigraphy with thallium (Tl^{201}) and technetium (Tc^{99m}).

4. Selective phlebography with catetherisation of thyroid plexus with determination of parathormone concentration.

5. Electrocardiography.

6. X-rays of a skeleton and kidneys.

7. Densitometry of bones.

8. The analysis of bone biopsy by means of quantitative histometry.

The diagnosis is based on data of the anamnesis, complaints, a clinical picture and results of additional tests. Constant attributes of hyperparathyroidism are hypercalciaemia, hypophosphatemia, increase of alkaline phosphatase in blood serum. Sometimes, hypomagnesemia, increase of chlorides (above 102 mmol/l), decrease in bicarbonates (hyperchloric acidose) are determined. The ratio of concentration of chlorides in blood and phosphates accounts for 33:1. There is an increase of excretion of calcium, phosphorus and hydroxyproline with urine, and also increased contents of interleukin-6 and the tumour necrosis factor in blood serum.

Differential diagnostics of hyperparathyroidism.

Conditions and diseases which are accompanied by development of hypercalciaemia are considered. There are 5 groups of diseases with hypercalciaemia:

1. Hypercalciaemia due to excessive secretion of parathormone:
   a) primary hyperparathyroidism;
   b) secondary hyperparathyroidism;
   c) tertiary hyperparathyroidism;
   d) multiple endocrine adenomatosis (MEA) I-st and II-th type;

f) hyperparathyroidism with ectopic production of parathormone (pseudoparathyperparathyroidism).

2. Endocrinopathic hypercalciamia:

a) thyrotoxicosis;

b) chronic adrenal insufficiency;

c) pheochromocytoma;

d) adenoma which secrets vasoactive intestinal peptide.

3. Malignant tumours:

a) osteolythic metastasis of malignant tumours in bones;

b) diseases of blood (leukaemia, lymphoma, lymphogranulomatosis, multiple myeloma).

4. Medicamentous hypercalciaemia:

a) alkalic-lactic syndrome;

b) treatment with thyazide diuretics;

c) overdose of vitamins A and D;

d) treatment by preparations of lithium;

f) treatment of breast cancer with estrogen, antioestrogen and testosterone.

5. Hypercalciaemia:

a) fractures of bones;

b) somatic diseases that keep patient in bed for a long term.

Secondary hyperparathyroidism is a compensatory response to prolonged hypocalcemia that develops due to disturbances of intestinal absorption (malabsorption syndrome) or rickets, Fanconi syndrome, and chronic renal failure. The content of calcium in the blood serum is normal or reduced (never increased), and the concentration of inorganic phosphorus is increased (renal secondary hyperparathyroidism form) or decreased (in case of secondary intestinal hyperparathyroidism).

Clinically secondary hyperparathyroidism appears with symptoms and attributes of the underlying disease. Paraesthesias of different localization can be observed along with typical spasms of muscles of hands or feet due to hypocalcemia. There is a weakness of muscles in proximal parts of extremities. Changes of a bone tissue include osteoporosis, osteosclerosis or fibrotic-cystic osteitis.

Continuous stimulation of the parathyroid glands by a combination of elevated extracellular phosphate concentration, decreased extracellular ionized calcium concentration, and markedly reduced serum calcitriol leads to increased parathormone synthesis and release. At the same time, elevated fibroblast growth factor 23 expression downregulates residual renal 25(OH)-1-hydroxylase, which exacerbates the effective deficiency of

calcitriol, acting as an additional driver to secondary hyperparathyroidism. Even at early stages in the development of hyperparathyroidism, these changes are compounded by variable underexpression of the calcium-sensing receptor and vitamin D receptor, rendering the parathyroid cells unable to respond appropriately to ambient calcium and/or calcitriol. The resulting increase in proliferative activity in the parathyroid glands eventually leads to parathyroid hyperplasia, which may get transformed to an adenoma with excessive secretion of parathormone.

Hypercalciaemic crisis is observed at primary and tertiary hyperparathyroidism, intoxications by vitamin D and hypercalcemia that is associated with malignant tumours. The increase of serum calcium above 3,49 mmol/L leads to the development of signs of calcium intoxication. The crisis develops when the level of serum calcium is above 3,99 mmol/L.

Hypercalcemic crisis is accompanied by anorexia, faintness, continuous vomiting, and pains in epigastric area, polydypsia, and polyuria. Later develops oliguria and anuria, dehydration, hypotonia of muscles and acute muscular weakness, pains in bones. Arterial hypertension might develop from the very beginning of crisis. The skin is dry, with scratch traces due to strong itch. Ligament reflexes are low. There are also psycho-neurologic signs: depression, mental confusion, coma, psychoses or psychomotor excitation. Anuria may develop, as well as cardiovascular insufficiency, inhibition of CNS, respiratory and vasomotor center depression, which may result in irreversible shock. Hypercalcemic crisis may be accompanied by severe gastrointestinal bleeding, development of intravascular thrombosis, disseminated intravascular coagulation syndrome.

Treatment of hyperparathyroidism
Indications for Treatment.

Removal of the abnormal and hyperfunctioning parathyroid tissue results in a long-term cure of hyperparathyroidism in 96% of patients and significant improvement in associated symptoms. The following criteria were proposed as indications for parathyroidectomy:
1. Serum Ca level more than 0,25 mmol/L above the upper limit of normal
2. Marked hypercalciuria higher than 400 mg/day
3. Creatinine clearance reduced more than 30% compared with age-matched controls
4. Reduction in bone mineral density of the femoral neck, lumbar spine, or distal radius of more than 2.5 standard deviations below peak bone mass (T score lower than -2.5)

5. Age younger than 50 years
6. Patients for whom medical surveillance is not desirable or possible
7. Presence of any complications (nephrolithiasis, overt bone disease)
8. An episode of hypercalcemic crisis

However, because no effective medical therapy for hyperparathyroidism exists, all patients with hyperparathyroidism who are otherwise healthy for surgery should be referred for surgical treatment.

Surgical Treatment.

Parathyroid surgery remains the single most effective treatment option in hyperparathyroidism and requires removal of all abnormal parathyroid tissue. Traditionally, this has meant bilateral exploration of the neck to identify all (typically four) parathyroids, assess which ones are abnormal, and remove only the abnormal glands. The setting of multiglandular hyperplasia requires subtotal parathyroidectomy or total parathyroidectomy, with reimplantation of parathyroid tissue into the sternocleidomastoid or forearm muscles. The parathyroids may then also be cryopreserved as a safeguard against future hypocalcemia, in which case the patient may undergo autotransplantation of autogenous, stored parathyroid tissue. In experienced hands, this approach has an exceptional rate of successful long-term cure of hyperparathyroidism (more than 96%) and a low rate of surgical complications (hypocalcemia less than 1%, recurrent laryngeal nerve injury 2% to 5%, neck hematoma or infection less than 1%).

Medical Treatment.

The need for treatment of hypercalcemia depends on the degree of hypercalcemia and the presence or absence of clinical symptoms. If calcium levels are lower than 3 mmol/L and a patient has no symptoms, it is unnecessary to treat the hypercalcemia. In patients with moderate calcium elevations (3 to 3.5 mmol/L) and symptoms consistent with hypercalcemia, aggressive treatment is necessary, whereas in those with moderate calcium level elevation but without symptoms, treatment may consist only of adequate hydration. Patients with calcium levels higher than 3.5 mmol/L should be treated aggressively, regardless of symptoms.

Measures undertaken to treat hypercalcemia may be divided into nonspecific therapies aimed mainly at increasing renal calcium excretion and decreasing intestinal absorption of calcium, those specifically aimed at slowing bone resorption, those directly removing calcium from circulation, and those aimed at controlling the underlying diseases causing hypercalcemia.

Calcium is passively reabsorbed by the favorable electrochemical gradient created by sodium and chloride reabsorption in the proximal tubule and in the thick ascending limb of the loop of Henle. Calcium is actively

reabsorbed via parathormone action in the distal tubule. Excretion of calcium can be achieved by inhibition of proximal tubular and loop sodium reabsorption. This is best achieved by volume expansion using an IV normal saline infusion (1 to 2 L for 1 hour). This will result in a marked increase in sodium, calcium, and water delivery to the loop of Henle. Using a loop diuretic (furosemide, 20 to 40 mg IV, every 2 hours) it is then possible to block transport of sodium in the loop. These actions will result in a marked increase in urinary excretion of calcium, but also of sodium, potassium, chloride, magnesium, and water. It is important to replace water, sodium, potassium, and chloride continuously and, if this regimen is prolonged for longer than 10 hours, to replace magnesium (15 mg/hr). Urinary flow should exceed 250 mL/hr during this time, and the serum calcium level will start decreasing within 2 to 4 hours and approach the normal range in 12 to 24 hours. Recurrent hypovolemia should be avoided.

In cases of hypercalcemia with high calcitriol levels, intestinal absorption may be the main mechanism responsible for hypercalcemia. Increased calcitriol production in cases with activated macrophages (granulomatous diseases and lymphomas) can be diminished using corticosteroids, 10 to 30 mg/day of prednisone, or higher in cases of lymphoma. If this is ineffective, ketoconazole, chloroquine, and hydroxychloroquine could be used to block calcitriol production.

Intestinal calcium absorption can be partially blocked by ingestion of phosphate-containing drugs (250 to 500 mg four times/day; the dosage should be adjusted to prevent diarrhea), which form insoluble calcium phosphate complexes and prevent absorption. Reducing calcium intake to 400 mg/day or lower is also beneficial.

When bone resorption is the main source of calcium, inhibition of this process results in lowering of the serum calcium level. Drugs used for this purpose include gallium nitrate, plicamycin (formerly mithramycin), calcitonin, and bisphosphonates. Gallium nitrate is potent but nephrotoxic, requires prolonged infusion (usually 5 days), and only limited experience with it exists in clinical practice. This compound cannot be recommended for routine use. Plicamycin use is limited by its toxicity, particularly in patients with renal, liver, or bone marrow disease. Calcitonin can be given subcutaneously or intramuscularly every 12 hours (4 IU/kg). Its action is rapid (4 to 6 hours), and the calcium level is usually lowered by 1 to 2 mg/dL. However, calcitonin is effective in only 60% to 70% of patients, and most of them develop tachyphylaxis in 48 to 72 hours, most likely because of receptor downregulation.

Bisphosphonates are a group of medications that accumulate in bone and powerfully inhibit osteoclast-mediated bone resorption. They

effectively lower the serum calcium level. Their maximum effect is seen in 2 to 4 days. The duration of effect is usually several weeks and varies among patients and with the type of bisphosphonate. Pamidronate, etidronate, alendronate, and zoledronate are currently available in the United States. Zoledronate appears to have the longest lasting effect (1 to 1.5 months), it is given in a 15-minute IV infusion (4 mg), and it is approved for use only in the hypercalcemia of malignancy. Pamidronate is used most commonly. It is given by IV infusion over 4 to 24 hours. The initial dose varies: 30 mg if the calcium level is lower than 3 mmol/L, 60 mg if the calcium level is 3 to 3.36 mmol/L, and 90 mg if the calcium level is above that level. A subsequent dose should not be given until after 7 days. Because of the lag in onset of effect, bisphosphonates should be combined with faster acting therapeutic modalities, such as IV saline infusion and calcitonin injections. Risedronate is another bisphosphonate that is currently being evaluated in oral form for the treatment of hypercalcemia. Bisphosphonates also appear to be promising in the prevention of hypercalcemia in patients with breast carcinomas.

Hemodialysis or peritoneal dialysis with low calcium levels in the dialysis fluid is effective for removing calcium from the circulation. These methods are used for patients with renal insufficiency and congestive heart failure when saline infusion is not feasible. Chelation of ionized calcium using ethylenediaminetetraacetic acid (EDTA) and IV phosphate has an immediate effect on calcium levels, but toxicity limits their use, and these methods have been almost abandoned.

HYPOPARATHYREOIDISM.

Hypoparathyroidism is the most common cause of hypocalcemia and often develops because of surgery in the central neck requiring radical resection of head and neck cancers. It develops in 1% to 2% of patients after total thyroidectomy. The hypocalcemia may be transient, permanent, or intermittent, as with vitamin D deficiency during the winter. Autoimmune hypoparathyroidism is seen as an isolated defect or as part of polyglandular autoimmune syndrome type I in association with adrenal insufficiency and mucocutaneous candidiasis. Most of these patients have autoantibodies directed against the calcium-sensing receptor. Congenital causes of hypocalcemia include activating mutations of calcium-sensing receptor, which has reset the calcium–parathyroid hormone relation to a lower serum calcium level. Mutations affecting intracellular processing of the pre-pro-parathormone molecule are also described and lead to hypoparathyroidism, hypocalcemia, or both. Finally, some cases are associated with hypoplasia or aplasia of the parathyroid glands; the best known is DiGeorge syndrome.

Pseudohypoparathyroidism is a group of disorders with postreceptor resistance to parathormone. One classic variant is Albright's hereditary osteodystrophy, associated with low stature, round facies, short digits, and mental retardation. Hypomagnesemia induces parathormone resistance and also affects parathormone production. Severe hypermagnesemia (>6 mg/dL) can lead to hypocalcemia by inhibiting parathormone secretion. Vitamin D deficiency leads to hypocalcemia when associated with decreased dietary calcium intake. The low calcium level stimulates parathormone secretion (secondary hyperparathyroidism), leading to hypophosphatemia.

Rhabdomyolysis and tumor lysis syndrome cause loss of calcium from the circulation when large amounts of intracellular phos-phate are released and precipitate calcium in bone and extraskeletal tissues. A similar mechanism causes hypocalcemia with phosphate administration.

Acute pancreatitis precipitates calcium as a soap in the abdomen, causing hypocalcemia. Hungry bone syndrome is hypocalcemia after surgery for hyperparathyroidism (HPT) in patients with severe prolonged disease (secondary or tertiary HPT in renal failure). Serum calcium is rapidly deposited into the bone. Hungry bone syndrome is rarely seen after correction of longstanding metabolic acidosis or after thyroidectomy for hyperthyroidism.

Several medications (ethylenediaminetetraacetic acid (EDTA), citrate present in transfused blood, lactate, foscarnet) chelate calcium in the circulation, sometimes producing hypocalcemia in which ionized calcium is decreased, cohereas total calcium may be normal. Extensive osteoblastic skeletal metastases (prostate and breast cancers) may also cause hypocalcemia. Chemotherapy, including cisplatin, 5-fluorouracil, and leucovorin, causes hypocalcemia mediated through hypomagnesemia. Hypocalcemia after surgery can be mediated by the citrate content of transfused blood or by a large volume of fluid administration and hypoalbuminemia. Patients with sepsis demonstrate hypocalcemia usually associated with hypoalbuminemia.

Clinical presentation

Chronic moderate hypocalcemia may be completely asymptomatic. Acute hypocalcemia causes increased neuromuscular irritability, underlying the most prominent symptoms. The clinical manifestation is tetany, repetitive neuromuscular discharge after a single stimulus. Tetany is seen in severe hypocalcemia (ionized Ca level lower than 1.1 mmol/L). Milder forms of neuromuscular irritability are paresthesias and numbness of the fingertips and perioral area. Twitching of the ipsilateral facial musculature (perioral, nasal, and eye muscles) by tapping over cranial nerve VII at the

ear is known as Chvostek's sign. Contraction at the oral angle alone is seen in 10% to 25% of the normal population. Trousseau's sign consists of carpal spasm provoked by ischemia, induced by inflation of the blood pressure measuring cuff around the arm, or alkalosis, provoked by hyperventilation. Spontaneous muscle cramps are commonly seen in hypocalcemia. Prolonged contraction of the respiratory and laryngeal muscles causes stridorous breathing and can cause cyanosis.

Neuropsychiatric Symptoms: Seizures, dementia (in adults), mental retardation (in children), emotional problems (anxiety, depression), extrapyramidal symptoms (parkinsonism is most common), calcifications of basal ganglia (in longstanding disease), papilledema.

Increased Neuromuscular Irritability: Chvostek's sign, Trousseau's sign, paresthesias in circumoral and acral areas (fingers, toes), muscle stiffness, myalgias, and spasms

Cardiovascular Symptoms: prolongation of QT interval, congestive heart failure, hypotension

Autonomic Symptoms: biliary colic, bronchospasm, diaphoresis

Other Symptoms: **c**ataracts, **d**ry coarse skin, dermatitis, hyperpigmentation, and eczema. Steatorrhea. Gastric achlorhydria.

Alkalosis (hyperventilation), hypokalemia, epinephrine (emotional stress), and hypomagnesemia aggravate symptoms of hypocalcemia, whereas acidosis diminishes symptoms; patients with chronic renal failure often tolerate marked hypocalcemia without symptoms.

Diagnosis

Hypocalcemia needs confirmation, if there is any doubt, by measurement of the serum ionized calcium level. When the diagnosis is confirmed by the finding of a serum calcium level lower than 2.05 mmol/L or an ionized calcium level lower than 1.1 mmol/L, attention should turn toward seeking the cause.

When no etiology is obvious, further testing is needed. Additional testing begins with serum concentrations of Mg, PO_4, parathormone (PTH), alkaline phosphatase, and occasionally vitamin D levels (25(OH)D, and 1,25(OH)$_2$D). Urinary PO_4 and cAMP concentrations are measured when pseudohypoparathyroidism is suspected.

PTH concentration should be measured as an assay of the intact molecule. Because hypocalcemia is the major stimulus for PTH secretion, PTH should be elevated in hypocalcemia.

- Low or even low-normal PTH concentrations are inappropriate and suggest hypoparathyroidism.

- An undetectable PTH concentration suggests idiopathic hypoparathyroidism.
- A high PTH concentration suggests pseudohypoparathyroidism or an abnormality of vitamin D metabolism.

Hypoparathyroidism is further characterized by high serum PO_4 and normal alkaline phosphatase.

In type I pseudohypoparathyroidism, despite the presence of a high concentration of circulating PTH, urinary cAMP and urinary PO_4 are absent. Provocative testing by injection of parathyroid extract or recombinant human PTH fails to raise serum or urinary cAMP. Patients with type Ia pseudohypoparathyroidism frequently also have skeletal abnormalities, including short stature and shortened 1st, 4th, and 5th metacarpals. Patients with type Ib disease have renal manifestations without skeletal abnormalities.

In vitamin D deficiency, osteomalacia or rickets may be present, usually with typical skeletal abnormalities on x-ray.

Treatment

Patients with acute symptomatic hypocalcemia (calcium level lower than 1.75 mmol/L, ionized calcium level lower than 0.8 mmol/L) should be treated promptly with IV calcium. Calcium gluconate is preferred over calcium chloride because it causes less tissue necrosis if extravasated. The first 100 to 200 mg of elemental calcium (1 to 2 g calcium gluconate) should be given over 10 to 20 minutes. Faster administration may result in cardiac dysfunction, even arrest. This should be followed by a slow calcium infusion, at 0.5 to 1.5 mg/kg/hr. Calcium infusion should continue until the patient is receiving effective doses of oral calcium and vitamin D. Calcium for infusion should be diluted in saline or dextrose solution to avoid vein irritation. The infusion should not contain bicarbonate or phosphate because this can form an insoluble calcium salt. If bicarbonate or phosphate administration is necessary, a separate IV line should be used.

Coexisting hypomagnesemia should be corrected in every patient. Care should be taken in patients with renal insufficiency because they cannot excrete excess magnesium. Magnesium is given via infusion and initiated with 2 g magnesium sulfate over 10 to 15 minutes, followed by 1 g/hr. In patients with severe hyperphosphatemia (tumor lysis syndrome, rhabdomyolysis, or chronic renal failure), treatment is focused on correcting the hyperphosphatemia.

Acute hyperphosphatemia usually resolves in patients with intact renal function. Phosphate excretion may be aided by saline infusion and acetazolamide, a carbonic anhydrase inhibitor, 10 to 15 mg/kg every 3 to 4 hours. Hemodialysis may be necessary for patients with symptomatic

hypocalcemia and hyperphosphatemia, especially if renal function is impaired. Chronic hyperphosphatemia is managed by a low-phosphate diet and use of phosphate binders with meals.

Chronic hypocalcemia (hypoparathyroidism) is treated by oral calcium administration and, if this is insufficient, vitamin D supplementation. The serum calcium level should be targeted to about 2 mmol/L. Most patients will be entirely asymptomatic at this level, and further elevation will lead to hypercalciuria because of the lack of PTH effect on the renal tubules. Chronic hypercalciuria carries the risks of nephrocalcinosis, nephrolithiasis, and renal impairment.

If oral calcium preparations cannot achieve adequate calcium repletion, vitamin D should be added. The usual initial daily dose is 50,000 IU of 25-hydroxyvitamin D (or 0.25 to 0.5 mg of 1,25-hydroxyvitamin D). Calcium and vitamin D doses are established by gradual titration. When adequate calcemia is achieved, urinary calcium excretion is measured. If hypercalciuria is detected, a thiazide diuretic may be added to diminish calciuria and further increase the serum calcium level. The serum calcium level should be monitored. If the phosphorus level is higher than 6.0 mg/dL when the calcium level is satisfactory, an unabsorbable phosphate binder should be added. Once controlled, the patient should be monitored every 3 to 6 months for calcium and phosphorus levels and for urinary calcium excretion.

Control of entry-level knowledge:
Task 1
The hyperfunction of the thyroid gland in diffuse toxic goiter is associated with:
a) hypersecretion of TSH,
b) hypersecretion of thyroliberin;
c) hyperproduction of thyroid stimulating immunoglobulins
Task 2
Which of the following studies are used for differential diagnosis between neurosis and diffuse toxic goiter?
a) test with TSH,
b) test with triiodothyronine**;**
c) test with potassium perchlorate;
d) uptake of I-131 by thyroid gland
Task 3
Which of these drugs affect the absorption of I^{131} by thyroid gland?
a) bromine preparations;
b) vitamin B**;**

c) enteroseptol;
d) asparkam

Task 4

The treatment of endemic diffuse goiter:

a) conservative;
b) surgical;
c) combined

Task 5

What is a purpose of scanning of thyroid gland?

a) determination of thyroid size;
b) determination of the functional state;
c) determination of tissue structure;
d) determination of the presence of nodes and their functional state

Task 6

What disease raises control of thyroid function by the hypothalamic-pituitary system?

a) endemic goitre;
b) primary hypothyroidism,
c) diffuse toxic goiter

Task 7

What is the age of patients who need prolonged drug therapy of diffuse toxic goiter and surgical treatment is done only by indication?

a) the elderly people with cardiac arrhythmias and coronary artery disease;
b) middle-aged persons;
c) children and adolescents;
d) age does not influence the choice of treatment

Task 8

What therapeutic dose of thyroxine is prescribed to patients with a normal level of TSH in the blood:

a) 2 mg / kg;
b) I mg / kg**;**
c) 0,5 mg / kg

Task 9

What should be the duration of antithyroid drug therapy in case of diffuse toxic goiter in order to achieve and maintain euthyroid state?

a) 3 months;
b) 6 months;
c) 1 - 1,5 years

Task 10

What are the complications of treatment with thyreostatics of imidazole group?
a) thrombocytopenia;
b) dyspeptic disorders;
c) leukopenia;
d) strumogenic effect;
e) all of the mentioned above

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

Control of final-level knowledge

Task 1

What are the common changes of complete blood count test in diffuse toxic goiter?
a) leukopenia;
b) accelerated erythrocyte sedimentation rate;
c) lymphocytosis;
d) all of the mentioned above

Task 2

The most optimal time for surgical treatment of diffuse toxic goiter during pregnancy is:
a) first 2 months;
b) end of the first and beginning of second trimester;
c) second trimester;
d) 3 trimester;
e) surgical treatment is not recommended

Task 3

Apathetic form of thyrotoxicosis is characterized by:
a) apathy, depression;
b) significant weight loss;
c) proximal myopathy, tremor;
d) arrhythmias;
e) all of the mentioned above

Task 4

What test can help to differentiate sporadic goiter from endemic?
a) level of T4 in blood;
b) the level of TSH in blood;
c) ultrasonography of thyroid gland;
d) daily urinary iodine excretion

Task 5

Which drug should be prescribed for treatment of endemic goiter of 3rd degree in elderly?

- a) antistrumine;
- **b) thyroxine;**
- **c) triiodothyronine;**
- d) thyreocomb

Task 6

Local myxedema is characterized by edema at the following locations of the body, except of:

- a) front surface of the tibia;
- b) waist;
- c) orbits of the eyes;
- d) hips

Task 7

What determines the severity of thyrotoxicosis?

a) enlargement of goiter;

b) degree of tachycardia;

c) dynamics of body mass

Task 8

The most informative examination of nodular goiter is:

- a) ultrasonography of thyroid gland;
- b) scanning of thyroid gland;
- c) fine needle biopsy;
- d) thermography;
- e) I^{131} uptake by thyroid gland

Task 9

A patient with compensated hyperthyroidism and progressive thyrotoxic ophthalmopathy is taking mercasolil. What necessary changes should be introduced to his treatment regimen? necessary:

a) to increase the dose of mercasolil;

b) to reduce the dose of mercasolil;

c) to prescribe lithium carbonate;

d) to prescribe glucocorticoids

Task 10

What is the optimal period for surgical treatment of diffuse toxic goiter in the presence of severe lesions of liver and heart?

a) after achieving euthyroid state;

b) 1 month after the compensation of thyrotoxicosis,

c) 2-3 months after the compensation of thyrotoxicosis

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

Tests

Task 1

What drug should be prescribed to a pregnant woman (12 weeks of gestation) after removal of the nodular goiter?

a) antistrumine;

b) thyroxine;

c) iodine preparations

Task 2

The main mechanism of antithyroid effect of glucocorticoids is:

a) changed sensitivity of thyrotrophs against thyroliberin;

b) reduction of transition of T4 to T3;

c) inhibition of thyroid stimulating antibodies formation;

d) reduction of steroid hormones synthesis;

e) blocked absorption of iodine by thyroid

Task 3

What is the reason for increased level of secretion of thyroid hormones?

A) mental and physical stress;

b) acute change in the temperature

c) eating disorders

Task 4

What tumors are often associated with nodular goiter?

a)   liver tumors;

b)   lung tumors;

b**)** uterine fibromyoma;

c) ovarian tumors;

d) breast tumors

Task 5

The classical presentation of congenital unrecognized hypothyroidism in children of 5-6 months old is:

a) delayed mental and physical development;

b) dysfunction of internal organs;

c) trophic changes of skin;

d) all of the mentioned above

Task 6

What can possibly cause the development of iatrogenic thyrotoxicosis?

a) overdose of thyroid hormones during treatment of hypothyroidism;
b) hypersensitivity of receptors to endogenous thyroid hormones;
c) all of the mentioned above

Task 7

The negative effect of β-adrenergic blockers on fetus in patients with diffuse toxic goiter is caused by:
a) teratogenic effects;
b) inhibition of cardiac excitation of the fetus;
c) inhibition of excitation of the respiratory center of the fetus;
d) damaging effect on the thyroid gland;
e) risk of hypothyroidism development

Task 8

Triiodothyronine thyrotoxicosis is characterized by:
a) increased level of T3 in the blood;
b) normal levels of T4 in the blood;
c) presence of both signs

Task 9

What blood pressure values are typical for uncomplicated diffuse toxic goiter?
a) increased systolic and diastolic pressure;
b) increased systolic and decreased diastolic pressure,
c) diastolic pressure is increased, while systolic is normal;
d) diastolic pressure is increased, while systolic is decreased;
e) both systolic and diastolic pressures are reduced

Task 10

What method is the most informative one for the diagnosis of ectopic goiter?
a) thermography;
b) radiography of the chest;
c) radioscopy of retrosternal space;
d) ultrasonography;
e) scanning with I^{131}.

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

Test questions:
1. The indicators of iodine metabolism
2. The methods for determination of the size of thyroid gland.

3. The definition of goiter.
4. The classification of goiter after Nikolaev (1955).
5. The classification of goiter by WHO (1992)
6. The definition of thyrotoxicosis.
7. The list of diseases that are accompanied by thyrotoxicosis.
8. Determination of diffuse toxic goiter (DTG).
9. The etiology, pathogenesis and clinical manifestations of diffuse toxic goiter.
10. Clinical syndromes that occur in patients with diffuse toxic goiter.
11. The lesion of thyroid gland in diffuse toxic goiter.
12. Thyroid cancer. Classification, clinical presentation, diagnosis and treatment.
13. The lesion of cardiovascular system in diffuse toxic goiter.
14. ECG changes in diffuse toxic goiter.
15. Psycho-emotional disturbances in diffuse toxic goiter.
16. Thyrotoxic encephalopathy in diffuse toxic goiter.
16. Thyrotoxic myopathy in diffuse toxic goiter.
17. Thyrotoxic myelopathy in diffuse toxic goiter.
18. Dysfunction of the gastrointestinal tract in diffuse toxic goiter.
19. Changes in the skin in diffuse toxic goiter.
20. Local myxedema.
21. Bone diseases in diffuse toxic goiter.
22. Thyrotoxic and endocrine ophthalmopathy.
23. Eye symptoms of thyrotoxicosis.
24. Thyrotoxic exophthalmos and its symptoms.
25. Symptoms caused by disturbance of oculomotor reaction: Wilder's, Mobius'; Graefe's, Popov's; Senton's; Kocher's.
26. Autoimmune ophthalmopathy.
27. Ocular symptoms of autoimmune ophthalmopathy.
27. Complications of autoimmune ophthalmopathy.
28. Signs of toxic goiter in children and elderly people.
29. Atypical variants of thyrotoxicosis: "apathetic" thyrotoxicosis and juvenile thyrotoxicosis.
30. Substantiation of diagnosis of thyrotoxicosis.
31. Diseases of parathyroid glands. Etiology, pathogenesis, clinical presentation, diagnosis, management.
32. Test of TSH.
33. Drug treatment of diffuse toxic goiter.
34. Surgical treatment of toxic goiter.
35. Therapeutic use of 131-iodine.
36. The indications for treatment with radioactive iodine.

37. Complications after treatment of goiter.
38. The indications for surgical treatment of diffuse toxic goiter.
39. Complication after surgical treatment of diffuse toxic goiter.
40. Side effects of thyrostatics.

Practical tests

1. To determine the degree of thyroid enlargement by palpation.
2. To identify the risk factors for diseases of thyroid gland, possible etiological factors; the initial signs of the disease; to assess the adequacy of diagnostic tests; to determine pharmacological anamnesis; to determine the main stages of the disease.
3. To substantiate the diagnosis of thyrotoxicosis.
4. To determine the nature of thyrotoxicosis complications.
5. To determine the presence and nature of ocular symptoms.
6. To assess the results of clinical, laboratory and instrumental examinations.
7. To determine the severity of thyrotoxicosis.
8. To make a differential diagnosis of goiter.

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