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Department of Internal Diseases № 2

Diffuse toxic goiter

Methodical materials

The main professional educational program of higher education - the specialty program in the specialty 31.05.01General medicine

Vladikavkaz

Methodical materials are designed to train students of 5 courses (9 semester) Therapeutic Faculty of FGBOU into the Sogma of the Ministry of Health of Russia in the Discipline "Endocrinology".

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EPIDEMIOLOGY

Diffuse toxic goiter (DTZ) (Bastedhouse-Graves disease, Parium disease) - a systemic autoimmune disease with a hereditary predisposition, which is based on the development of stimulating autoantibodes to TSH receptors located on thyroidocytes, clinically manifested by the thyroid lesion (imagine) with the development of thyrotoxicosis syndrome In combination with extractoreroidal pathology (Endocrine ophthalmopathy (EEO), prematible mixedma, acopathy). The combination of all components of the system autoimmune process is relatively rare and is not bond for diagnosis. In most cases, the largest clinical significance in Greiva's disease (BG) has the defeat of the pin . The disease was first described by Robert James Graves in 1835 in Dublin (Ireland), and in 1840-monetsky doctor Carl Adolf von Basnedovs Merzeburg (Germany) ("Merzeburg Creator Bastedov" - Exophthalm, Tachycardia, Goob).

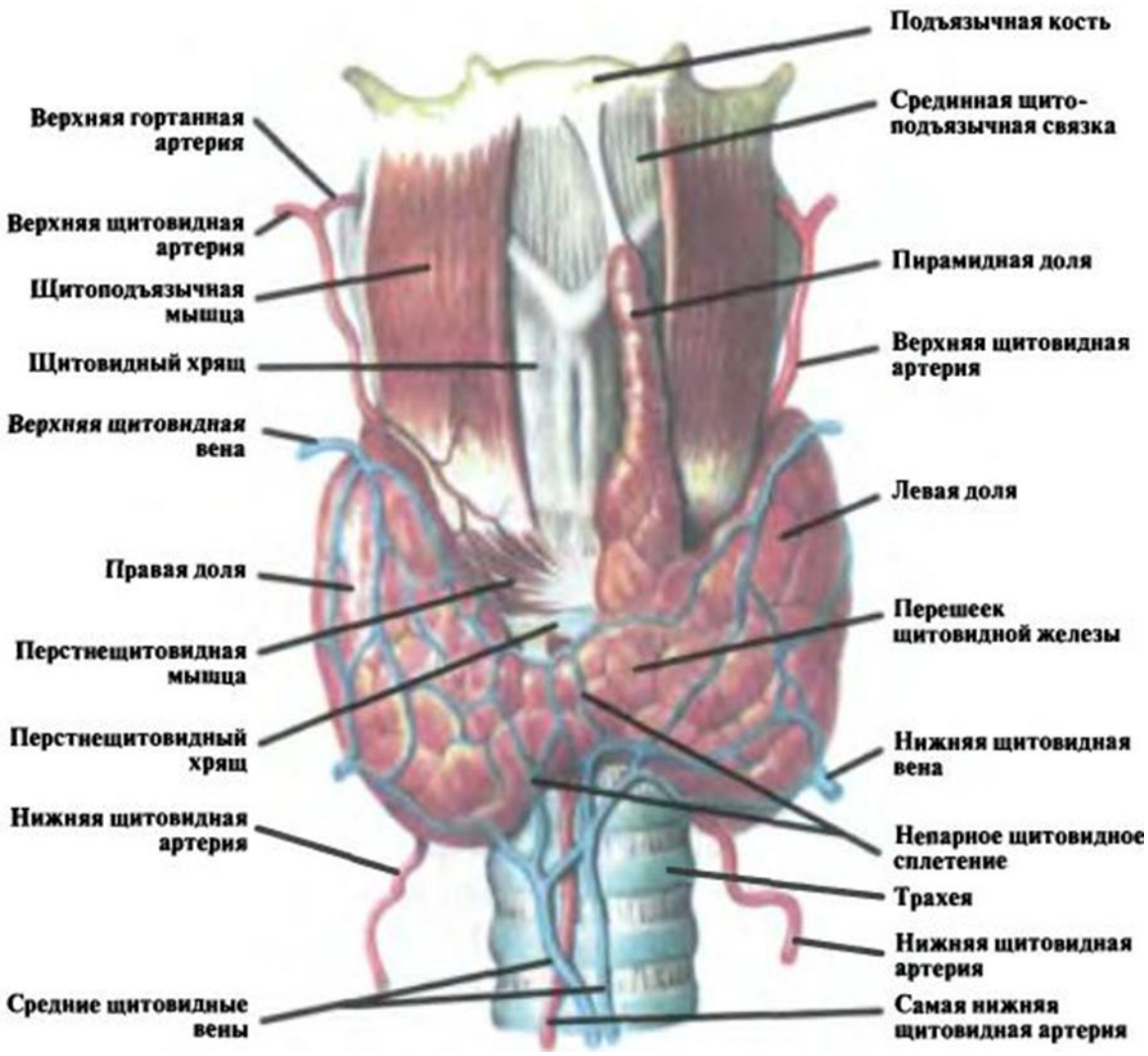
Women get sick of BGV 10-20 times more often, the disease falls on a young and middle age. In regions with normal support, BG is the most common cause of resistant thyrotoxicosis, and in iodine deficient regions, in the etiological structure of toxic goiter, it bgccorates with a functional autonomation (nodular and multi-nose toxicosis). Diffuse toxic goiter is up to 80% of all cases of hyperfunction. But the problem of thyrotoxicosis is determined not so much of its prevalence as the severity of consequences: affecting metabolic processes, it leads to the development of severe changes in many systems of the body (cardiovascular, nervous, digestive, reproductive, etc.).

In Russia, as synonymous with the term "Graves Disease" ("Basedov Disease"), the term "diffuse toxic goiter" is traditionally used, which is not deprived of a number of significant flaws. Overseas, it characterizes only a macroscopic (diff-function goiter) and a functional (toxic) change of a chance that is not equivalent to a graves' disease: from one SSTONER, an increase in the gland may not be, on the other, the goiter may not be diffuse. Secondly, the diffuse increase in the threshold in combination with thyrotoxicosis may occur with other diseases, in particular the so-called diffuse functional autonomy. Using the incomplete term "disease" (and not simply "toxic goiter") in relation to the disease under discussion, most likely, becoming more or more unrecognizable systemicity of the autoimmunogoprocess. In addition, the term "Graves Disease" is most often used worldwide, and in the German-speaking officers - Basnedov disease.

Anatomy and thyroid physiology

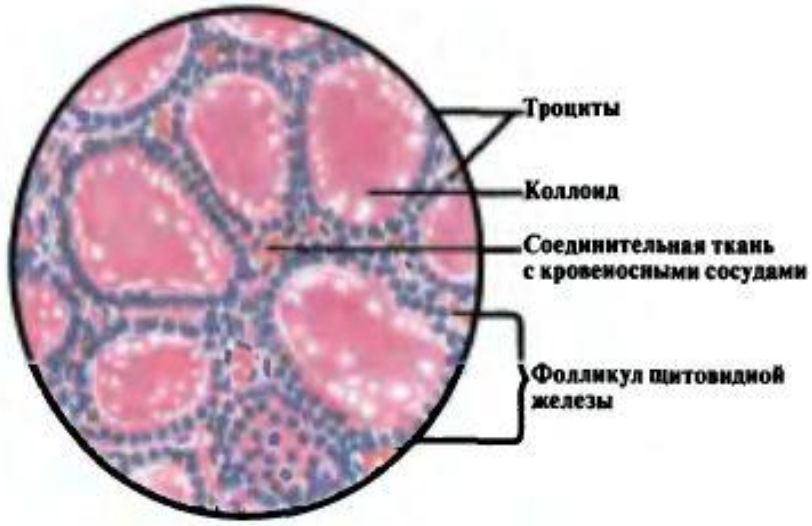
The thyroid gland (imagine) is the largest endocrine iron of the human body, which has only intrasecreteral function. The thyroid gland is located on the front surface of the neck, covering the front and sides of the sides of the Top Rings of the trachea, its weight in an adult is about 15-20 g. Being a horsesholic form, it consists of two pieces and a carriage located on the front surface of the trachea and on its sides (Fig. 1). Sometimes an additional pyramidal share is departed from the car. The pin is developing from the middle of the middle of the primary pharynx. The thyroid gland laying occurs on the 3-5 week of embryonic development, and from 10-12 weeks it acquires the ability to capture iodine, by 18-20 weeks it begins to produce thyroid hormones. In case of imbigenesis, various anomaly of its location may develop. These include cysts of a securing duct, the paternal sput, as well as the median and side remains of thyroid tissue.

Fig.1 Thyroid gland



The brush consists of cells of two different types: follicular and parapollicular (C-cells). Follicular cells producing thyroxine (T4) and triiodothyronine (TK) are formed in the gland numerous follicles, each of which consists of a central cavity filled with a colloid, the main component of which is a protein of thyroglobulin, surrounded by one layer of cuboid epithelial cells (Fig. 2). Parapollicular cells (C-cells) produce a squitonin protein hormone.

Fig.2 Histological structure of the thyroid gland



The necessary structural component of thyroid hormones is iodine. This trace element is almost completely absorbed in the intestines, from where in the ionized form enters the blood plasma. Iodine transfer inside the Tyrocyte is energy-dependent and carried out by conjugate transportation of sodium sodium-iodidnysimporter (NIS). In the iodine ion cells oxidizes, after which the organicles are exposed, joining the residues of tyrosine amino acid molecules, which are present in thyreoglobulin, synthesized by follicular cells. After that, thyroglobulin changes its structure in such a way that the tyrosal residues come together with each other, facilitating the condensation reaction between them. The iodization of tyrosyl residues and the condensation reaction occurs with the participation of thyroid-peroxidase of the thyroid gland (TPO) localized in the microsomal fraction of follicular cells. Next, containing associated yodththinosyroglobulin is transported through the apical membrane, vertical membranes are transferred, moves to their basal membrane, releases uodththnic, which are highlighted in blood. Finding into the blood, the T4 IT3 is distributed by the body mainly in plasma proteins associated with proteins (thyroxins binding globulin, prehaletbin (transstirtin), albumin). The half-life period for T4 is 7-9 days, for T3 - 2 days.

Free yodthnins relatively easily penetrate through the cell membrane. The intracellular effects of thyroid hormones are closely related to the processes of their metabolism (primarily with the mechanisms of the event). The most important of these transformations is T4 conversion to more active T3. Since with thyroid hormone receptors directly interacts mainly T3, and not T4, the latter is customary to be considered as a corrugated, and T3 - as a true hormone. The TK effect on specific nuclear receptors, which are present by cells, leads to a change in the expression of various genes, which is manifested by the physiological effects of thyroid hormones, the main of which is regulation and maintaining the main exchange. Only 5-10% of the blood circulating T3 is synthesized directly by the pin; Its most is formed as a result of the T4 case in peripheral tissues. The conversion (conversion) T4 in T3 is catalyzed by various databases with tissue specificity.

The regulation of the function of the thyroid gland is under the control of the hypothalamus producing the thyrotropin-rillation factor (thyareoliberin), under the influence of which the thyrotropic hypostic hormone (TSH) is released, stimulating the production of thyroid iron T3 and T4. There is a negative feedback between the level of thyroid hormones in the blood and TSH, due to which their optimal blood concentration is maintained.

The role of thyroid hormones:

• increase the sensitivity of adrenoreceptors, increasing the frequency of heart abbreviations (heart rate), blood pressure;

• on the intrauterine stage contribute to the differentiation of tissues (nervous, cardiovascular, musculoskeletal systems), during the periods of childhood - the establishment of mental activities;

• Increase oxygen consumption and main exchange level:

o activating protein synthesis (including enzymes);

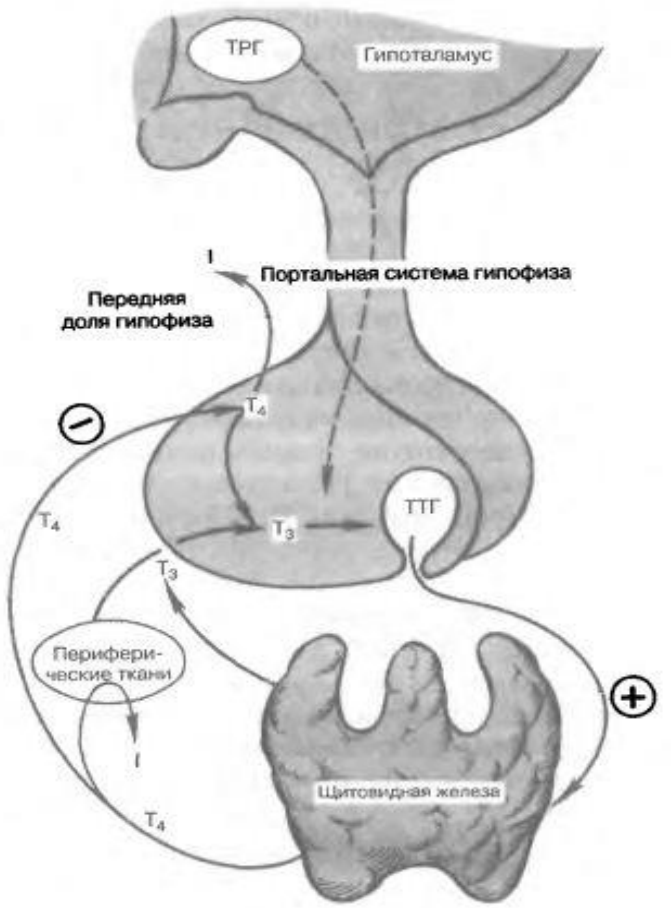
o increasing the seizure of calcium ions from blood;

o activating glycogenolysis, lipolysis, proteolysis;

o contributing to the transport of glucose and amino acids into the cell;

o increasing the heat product.

Fig. 3. Regulation of secretion of thyroid hormones



ETIOLOGY

To date, it has been almost obvious that the last stage of the pathogenesis of Greiva's disease is the developing formulating immunoglobulins (TSI), which are associated with receptorTG (RTTG) and activate it. Many immunological aspects of grave sickness with such a classic autoimmune thyroid (autoimmune hypothyroidism), and these diseases in some cases are experiencing in the same family.

At the same time, factors that determine the development of various embodiments of an autoimmune disease of the threshold in persons with similar genetic predisposition, to date remain unknown.

Genetic factors

The detection of circulating autoantibodies in 50% of DTZ relatives, frequent detection in HLA DR3 haplotype patients with other autoimmune diseases, is evidenced about the genetic susceptibility. The combination of DTZs with autoimmune chronic adrenal insufficiency, type 1 diabetes, as well as other autoimmune endocrinopathies is denoted as an autoimmune polyglandular type 2

syndrome. Hereditary predisposition under the action of trigger factors (viral infection, stress, etc.) leads to the appearance in the body of thyroid-formulating immunoglobulins - LATS factors (longactionThyreoidstimulator, a long-acting thyroid stimulator). When entering into cooperation with receptors to thyrotropic hormone on thyroidocytes, thyroidistimulating antibodies cause an increase in the synthesis of hormones T4 and T3, which leads to the appearance of the state of thyrotoxicosis.

Environmental factors

Patients with graves disease on stressful events in the life, which happened during the last year, indicate more often, the odders included in the control group that all the same, not fully evidenced by the role of stress in the pathogenesis of this disease.

A significant increase in consumption in the iodine deficit regions, on the one hand, can lead to an increase in the incidence of thyrotoxicosis due to the decompression of the functional autonomycling and, on the other hand, to accelerate the manifestation of Graves's disease in predisposed persons. Smoking has a weak association with an increase in graves disease increment, but at the same time is the most important risk factor for the manifestation and progression of the endocrine ophthal-moat (EEO). With a scientific position, the yatrogenic causes contributing to the development of Greiva's disease are of great interest. In particular, several cases of disease development Against the background of the appointment of immunomodulators, such as βinteroneon (β-IFN), and on the background of intensive antiretroviral therapy (and in clinical practice it is necessary to differentiate a graves with a thyrotoxic phase of α substationin-chirmed, which on the background of therapy with interferon drugs is developing significantly more often than boasigngerevs). An equally interesting example is the development of a third of the third patients with multiple sclerosis, which are treated with monoclonal antibodies to tttchlets. In this case, the induction of an autoimmune response can be in the pathogenesis of the disease, due to the shift of the th1 / TH2 coordination or changes with part-pull cells. Another example of induced immunological shift in principle could be the simultaneous formation of graves and allergic diseases. This testifies to the fact that the TH2-response is an unfriendly indicator. These data and are attractive to the fact that potentially intervening the immunoregulatory processes, it would be possible to achieve the remission of graves disease, however, it carries a hidden threat of inductors of TH1-dependent diseases, such as sclerosis and type 1 diabetes mellitus.

Antibodies to the TTG receptor

The existing nomenclature of antibodies to the TTG receptor (AT-RTTH) created some confusion. Cloning-RTTH significantly advanced our ideas about the principles of the interaction of antigen and antibodies and made it possible to create a significantly more advanced test system. However, the complete understanding of the structural and functional relations of the AT-RTTH with the receptor itself is not achieved due to the fact that there are no monoclonal antibodies to human course. In addition, there is no acceptable systems for the definition of stimulating antibodies to the RTTG (in contrast to antibodies that can simply contact the RTTG). Another problem is that, despite the significant efforts taken in this direction, today there is no adequate animal model that would fully comply with Greivs disease.

The TTG receptor is a molecule associated with G-protein, which consists of 379 amino acids of Etodomena, 7 associated with a diaphragm of chains and a short intracellular tail. The assembly of the receptor is carried out due to the splitting of a single chain synthesized on the membrane on A- and V-subunits with a loss of about 50 amino acids from the C-terminus. The subunit agrees most of the ectodomena, and the sub alone is the rest of the receptor, after which the disulfide bridges are connected. Subunit A in the culture of thyroidocyte over the surface and can be isolated and chemically stabilized by this form in which it will react with antibodies and, thus, can be used to determine them.

Antibodies that stimulate the RTTG are binding exclusively with the N-terminal fragment of its molecule, and those antibodies that block the receptor preventing binding from TSH is exclusively with a C-terminal fragment, while the epitopidation of those for other antibodies is largely superimposed Most of each other, and the degree of this imposition may depend on the conformational changes of the entire protein. Published data on what the third version of the binding of antibodies with the receptor can also exist in which the antibody connects without any functional consequences. Therefore, antibodies may exist, which can further be detected by newer methods in patients who have not previously defined these antibodies. Taking into account the possibility of alternating products of various options at AT-RTTG, it becomes clear that the RTTG and antibodies to it have exceptional and unusual properties, the study of which will bring us to the clarification of the pathogenesis of Greiva disease.

Other Components of the Immunist Answer

During graves, a polyclonal-cell response is found in the clutch, the micro-mechanogenicity of the transcripts of the T-lymphocyte receptor of the receptor V. is detected. And we are talking about heterogeneity of both T-cells and autoantigen

briefs. Up to 80% of patients with graves themselves antibodies (and, consequently, CD4 + T cells), which react with thyroid-peroxidase (ATTPO). With a slightly lower frequency there are antibodies to thyroglobulin (ATTG).

The brief itself is a place where the synthesis of autoantibodies is carried out, but only in the later stages of the disease. At the same time, it is not quite clear how the cattockin profile is Th1 or Th2 - can be expertly expected, which is probably due to a large duration and a variety of autoimmune response. The sput cells themselves express a number of pro-inflammatory molecules in response to the action of cytokines and sub-paltal attackclosure elements that can occur during Greus disease. As a result, thyarocyte itself can affect the progression of the autoimmune process. Apparently, the individual features of the regulation of these interactions are at least one sourcemanmannant of a different clinical course of Greiva's disease, in particular its severity, the degree of increasing the imaging and the forecast of the effectiveness of thyaretic therapy.

Clinical picture

The classical Merzeburg Triad (goiter, tachycardia, exophthalm), described by Karl Basedov, is occupied about 50% of patients.

As mentioned, the clinical picture of the BG is determined by the syndrome of the thermotoxicosis for which weight loss is characterized, often against the background of elevated appetite, sweating, tachycardia and sensation of the heart, inner concern, nervousness, trembling hands, and sometimes the body. In elderly patients, thyrotoxicosis of any genesis often flows oligo or monosimptomino (evening subfebelitet, arrhythmias) or even atypically (anorexia, neurological symptoms). A false study is about 80% of patients, it is possible to identify an increase in the brush, sometimes very significant.

In some cases, when the BG on the first place is the manifestations of the EOP. It should be noted here that the patient has a pronounced eope allows you to almost unmistakably establish a patient with an etiological diagnosis already under the clinical picture, since among the diseases occurring with thyrotoxicosis, the ESO is combined only with BG.

Nervous system. The damage to the nervous system with thyrotoxicosis arises almost always, so before it was called "neurotyrea" or "thyreonosis". In the pathological process, the central nervous system, peripheral nerves and muscles are involved.

The effect of excess thyroid hormones primarily leads to the development of neurasthenic symptoms. Complaints of increased excitability, anxiety, irritability, obsessive fears, insomnia, there is a change in behavior - fussiness, fiscalness, excessive motor activity, loss of ability to concentrate attention (the patient switches sharply from one thought to another), emotional instability with a quick change of mood from an advention before depression. True psychosis is rare. Inability and depression syndrome called "apathetic thyrotoxicosis", usually occurs in the elderly patients. Fobic manifestations are very characteristic of thyrotoxicosis. Cordiophobia, claustrophobia, sociophobia, often occurs.

In response to a physical and emotional load, panic attacks occur, manifest themselves with a sharp increase in the pulse, an increase in blood pressure, by pale of the skin, dryness in the mouth, a chill-like shake, fear of death.

Neurotic symptoms for thyrotoxicosis are nonspecific, and with the development and weight gain of the disease, we fill, by changing the heavy organs.

Tremor - early symptom of thyrotoxicosis. This hyperkinosis remains alone, and when driving, and the emotional provocation enhances its severity. Tremor captures his hands (symptom of Marie - tremor fingers of elongated hands), eyelids, tongue, and sometimes the whole body ("symptom of a telegraph pillar"). Shivery constant, it prevents work, write, draw.

As the disease is raising, fast fatigue, muscle weakness, diffuse weight loss, muscle atrophy is progress. In some patients, muscle weakness reaches extremely severity and even leads to death. Extremely rarely, with severe thyrotoxicosis, the seizures of generalized muscle weakness (periodic thyrotoxic hypokalemic paralysis), exciting muscles of the body and limbs, including respiratory muscles, can suddenly occur. In some cases, paralysis is preceded by attacks of weaknesses in the legs, paresthesia, pathological fatigue muscles. Paralysis develops violently. Such attacks can sometimes be the only manifestation of thyrotoxicosis. In terms of electromyography, polyfias are detected in patients with periodic paralysis, reducing the potentials of action, the presence of spontaneous activity of muscle fibers and bezkiculation.

Chronic thyrotoxic myopathy occurs with the long flow of thyrotoxicosis, is characterized by progressive weakness and fatigue in proximal groups of muscles of the limbs, more often. Difficulties are noted when climbing the stairs, getting up from the chair, combing hair. Gradually develops symmetric hypotrophy muscles of the proximal sections of the limbs.

The cardiovascular system. The most important target organ with violations of the function of the thyroid gland is the heart. In 1899, R. Kraus introduced the term "thyrotoxic heart", under which the symptom complex of violations of the activity of the cardiovascular system caused by a toxic effect of excess thyroid hormones characterized by the development of hyperfunction, hypertrophy, dystrophy, cardiosclerosis and heart failure.

The pathogenesis of cardiovascular disorders with thyrotoxicosis is associated with the ability of TG directly to contact cardiomyocytes, providing a positive inotropic effect. In addition, increasing the sensitivity and expression of adrenoreceptors, thyroid hormones cause significant changes in hemodynamics and the development of acute heart pathology, especially in patients with ischemic heart disease (Fig. 4). The increase in heart rate, increase the impact volume (UO) and a minute volume (MO), acceleration of blood flow, a decrease in the total and peripheral resistance of the vessels (OPS), a change in blood pressure. Systolic pressure moderately increases, the diastolic remains normal or reduced, as a result of which the pulse pressure increases. In addition to the listed thyrotoxicosis, an increase in the volume of circulating blood (BCC) and the erythrocyte mass is accompanied. The reason for the increase in the OCC is the change in the serum level of erythropoietin in accordance with the change in the serum level of thyroxine, which leads to an increase in the mass of red blood cells. As a result of an increase in the minute volume and mass of circulating blood, on the one hand, and reducing peripheral resistance, on the other, the pulse pressure and the load on the heart in diastole are increased.

The main clinical manifestations of heart pathology with thyrotoxicosis are sinus tachycardia, atrial flications (MP), heart failure and metabolic shape of angina. In the case of a patient a heart disease (IBS), hypertensive disease, heart defects, thyrotoxicosis only accelerate the emergence of arrhythmias. There is a direct dependence of MP on the severity and duration of the disease.

The main feature of sinus tachycardia is that it does not disappear during sleep and insignificant physical exertion dramatically increases the frequency of heart abbreviations. In rare cases, sinus bradycardia is found. This may be due to congenital changes either with the depletion of the function of the sinus node with the development of its weakness syndrome. Atrial flicker is found in 10-22% of cases, with the frequency of this pathology increases with age. At the beginning of the disease, atrial flications wears paroxysmal character, and the progression of thyrotoxicosis can move into a permanent form. In patients of young age, without

concomitant cardiovascular pathology after subtotal resection of the thyroid gland or successful thyaretic therapy, a sinus rhythm is restored.

In the pathogenesis of the atrial flickering, a violation of an electrolyte balance plays an important role, more precisely, the decrease in the level of intracellular potassium in myocardium, as well as the depletion of the nostropic function of the sinus node, which leads to its depletion and transition to the pathological rhythm.

For thyrotoxicosis, atrial violations of the rhythm are more characteristic, and the appearance of ventricular arrhythmia is characteristic only for severe form. This may be associated with a higher atrial sensitivity to the arrhythmogenic action of TSH compared to ventricles, since the density of beta-adrenoreceptors in the atrial tissue prevails. As a rule, ventricular arrhythmias are found when combining thyrotoxicosis with cardiovascular diseases. At the occurrence of the stealth, they are saved.

Digestive system. Food consumption increases, in some patients there is an uncompripable appetite. Despite this, patients are usually thin (patients can lose weight to 10-15 kg per month with an increased appetite). Complete thyroid hormones reinforce heat products, and heat transfer at the expense of sweating, which leads to a light polydipsy. For older patients, anorexia is characteristic. Due to the enhancement of the peristaltics, Chair is frequent, which is associated with the enhancement of the motor function of the gastrointestinal tract, which leads to impairment of suction primarily in greasy acids. Finding into a fat intestine, they cause strengthening secretion. The absorption of other nutrients increases the osmolarity of the contents of the small intestine, accompanied by the development of osmotic diarrhea. However, the pronounced digestion disorders during thyrotoxicosis is not noted.

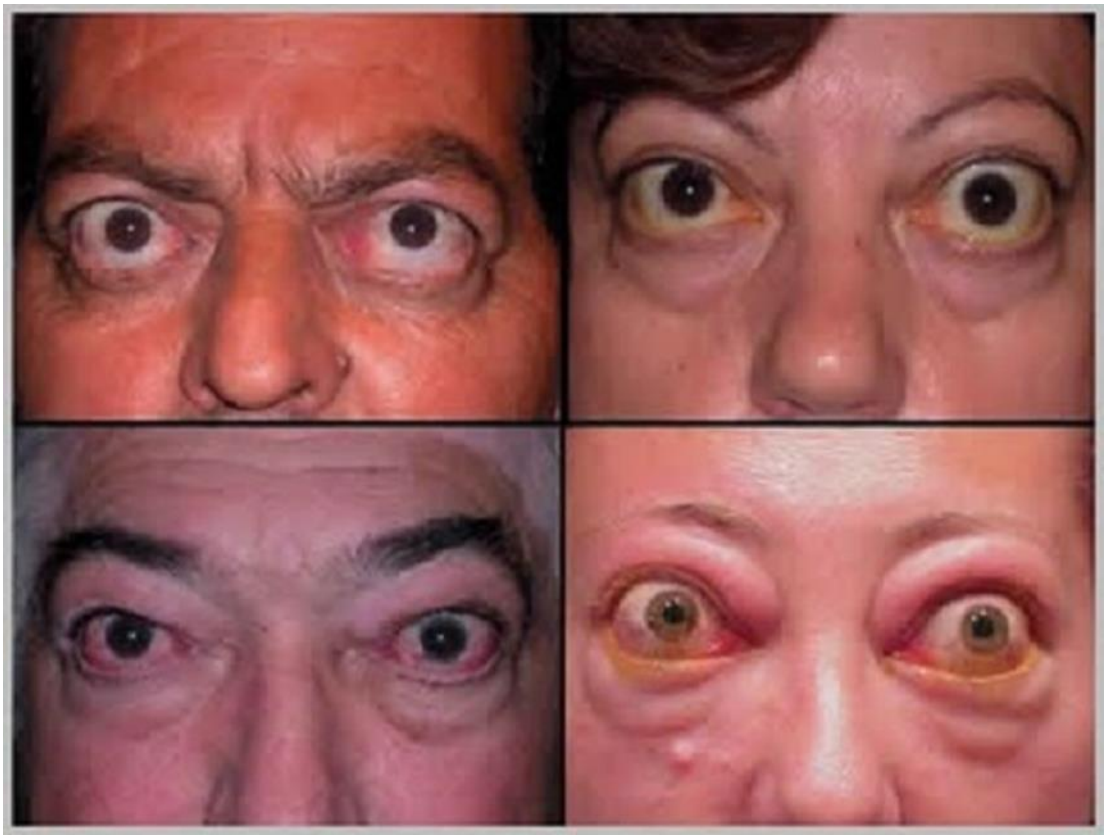
Thyareoxic Exophthalm. Thyareoxic Exophthalm is always found against the background of thyrotoxicosis, more often in women. The eye slot in such patients is open, although there is no exophthalma, or it does not exceed 2 mm. An increase in the eye cracking occurs due to the retraction of the upper eyelid. Other symptoms can be detected: when viewed, it is sometimes visible a strip of a sclera between the upper century and the iris (Symptom of Ralemple). When looking down, lowering the upper eyelid lags behind the movement of the eyeball (symptom of the Gref). These symptoms are due to an increase in the tone of smooth muscles raising the upper eyelid. It is characterized by a rare flashing (Schutellum symptom), a gentle tremor of the eyelids in their closure, but the eyelids are completely closed (tab. 1.) The volume of movements of extracular muscles is not disturbed, the eye continuous remains normal, the function of the

eye does not suffer. The reposition of the eye is not difficult. The use of instrumental research methods, including computed tomography and nuclear magnetic resonance, proves the lack of changes in the soft tissues of the orbit. The symptoms described are disappearing against the background of drugs of the thyroid dysfunction.

Eye symptoms of thyrotoxicosis should be distinguished from independent disease of endocrineophalmopathy.

Endocrineophalmopathy (Graves) is a disease due to the damage to the periorubital tissues of autoimmune genesis, which in 95% of cases is combined with autoimmune diseases of the thyroid gland. It is based on lymphocytic infiltration of all the formations of the eye and retroorbital swelling. The main symptom of ophthalmopathyagreus - Exophthalm (Fig. 5.). Edema and fibrosis of the ice muscles lead to the limitation of the mobility of the eyeball and diplopia. Patients complain of rubber in their eyes, light, tear. Because of the immeasures of the eyelid, the cornea dries and can ulcerate. The compression of the optic nerve and keratitis can lead to blindness.

Fig. 5. Endocrine ophthalmopathy.



Sex system. Thyrotoxicosis in women reduces fertility and can cause oligomenore. Men suppressed spermatogenesis, occasionally reduced potency. Sometimes

gynecomastia is observed due to the accelerated peripheral transformation of androgen in estrogens (despite the high level of testosterone). Thyroid hormones increase the concentration of globulin binding sex hormones, and thereby increase the total content of testosterone and estradiol; At the same time, the levels of luteinizing hormone (LH) and the follicular-wing hormone (FSH) in serum can be both elevated and normal.

Musculoskeletal system. The strengthening of catabolism leads to weakness and muscle atrophy (thyrotoxic myopathy). Patients look exhausted. Muscular weakness manifests itself when walking, lifting uphill, getting up with knees or lifting weights. In rare cases, there is a transient thyrotoxic paralysis, which lasts from a few minutes to several days.

Increased level of thyroid hormones leads to a negative mineral balance with loss of calcium, which is manifested by reinforced bone resorption and reduced intestinal suction of this mineral. Resorption of bone tissue prevails over its formation, so the calcium concentration in the urine is increased.

In patients with hyperthyroidism, low levels of vitamin D-1.25 metabolite (O) 2D are found, sometimes hypercalcemia and a reduction in the level of pararathgamon in serum. Clinically, all these violations lead to the development of diffuse osteoporosis. Pains in the bones, pathological fractures, the collapse of the vertebrae, the formation of kyphosis is possible. Arthropathy for thyrotoxicosis is rarely developed, by type of hypertrophic absorpathy, with thickening the phalange of the fingers and periosal reactions.

Thyarecic crisis is a sharp exacerbation of all symptoms of thyrotoxicosis, being a severe complication of the underlying disease accompanied by hyperfunction of the thyroid gland (in clinical practice it is usually toxic goiter). The following factors contribute to the development of the crisis:

• Long absence of treatment of thyrotoxicosis;

• Intercurrent infectious inflammatory processes;

• severe mental injury;

• significant physical exertion;

• operational treatment of any nature;

• treatment of toxic goiter with radioactive iodine, as well as surgical treatment of the disease, if the eutheroid state is not previously reached; In this case, as a result

of massive destruction of the thyroid gland, a large amount of thyroid hormones is distinguished.

The pathogenesis of the crisis is excessive admission to the blood of thyroid hormones and the heavy toxic damage to the cardiovascular system, the liver, the nervous system and the adrenal glands. In the clinical picture, a sharp arousal is characterized (up to psychosis with nonsense and hallucinations), which is then replaced by adamisia, drowsiness, muscle weakness, apathy. When inspection: The face is sharply hypertic; Eyes widely disclosed (expressed exophthalm), blinking rare; profuse sweating, in the future replacing the dryness of the skin due to pronounced dehydration; Skin hot, hyperemic; High body temperature (up to 41-42 ° C).

High systolic blood pressure (AD), diastolic blood pressure reduced significantly, with a far-seated crisis systolic blood pressure decreases sharply, the development of acute cardiovascular failure is possible; Tachycardia to 200 strikes per minute goes to the flicker of the atria; Disposal disorders increase: thirst, nausea, vomiting, liquid chair. There may be an increase in the liver and the development of jaundice. Further progression of the crisis leads to loss of orientation, symptoms of acute adrenal insufficiency. Clinical symptoms of the crisis are more often increasing for several hours. In the blood of TTH may not be determined, the level of T4 and T3 is very high. Hyperglycemia is observed, urea, nitrogen values increase, the acid-base state and the electrolyte composition of the blood is changed - the potassium level is increased, sodium - falls. It is characterized by leukocytosis with a neutrophilic shift to the left.

DIAGNOSTICS

In typical cases, the diagnosis of BG does not have significant difficulties. In case of suspected the presence of thyrotoxicosis in the patient, it shows it determining the level of TSH highly sensitive method (functional sensitivity of at least 0.01 honey / l).

When the reduced level of TSH, the patient is determined to determine the level of SV. T4 and sv. T3. The modern laboratory methods allow you to diagnose two versions of thyrotoxicosis, which are very often stages of the same process:

• Subclinical thyrotoxicosis: is characterized by a decrease in the level of TSG in

Combined with normal levels of free T4 and free T3.

• Manifestic (explicit) thyrotoxicosis is characterized by a decrease in TSH levels and an increase in the level of free T4 and free T3.

Thyroglobulin. Increasing the level of thyreoglobulin in serum is detected at various forms of thyrotoxicosis: diffuse toxic zob, subacute and autoimmune thyroid, multi-nose toxic and non-toxic zob, endemic zob, thyroid cancer and its metastases. For medullary thyroid cancer, a normal or even reduced content of thyreoglobulin in blood serum is characteristic. With thyroiditis, the concentration of thyroglobulin in serum may not correspond to the degree of clinical symptoms of thyrotoxicosis.

Suppressive samples with T3 or T4. With thyrotoxicosis, the absorption of radioactive iodine with a thyroid gland under the influence of exogenous thyroid hormones (3 mg of Levothyroxine is once inside or 75 μg / sublimine inside for 8 days) does not decrease. Recently, this sample is rarely used, since highly sensitive methods for determining TSH and the methods of scintigraphy-shaped gland are developed. The sample is contraindicated in diseases of the heart and the elderly patient.

After confirming the presence of thyrotoxicosis in the patient, etiological diagnostics are carried out, aimed at identifying a specific disease, which has led to it. When bg, with an ultrasound, an area of 80% of cases, a diffuse increase in the bridge is detected. The ultrasonic picture in BG does not have specific features and is characteristic of most autoimmune diseases of the brush.

Radionuclide scanning. The functional state of the thyroid gland can be determined in the test with the capture of the radiopharmaceutical frame (radioactive iodine or the peckenet technique). When using the Iodine Iodine isotope, the iodine is captured, visible on the scintigrame. Non-functioning areas are not visualized and called "cold". The thyroid scintigraphy is carried out in patients with thyrotoxicosis and nodal goiter to find out:

o Is there an autonomous hyperfunctioning unit, which accumulates the entire radioactive iodine and suppresses the function of normal thyroid tissue.

o Are there multiple nodes that accumulate iodine.

o Are palpable nodes with cold (hyperfunctioning fabric is located between the nodes).

As with other autoimmune diseases of the threshold, the BG may determine the high levels of classical anti-ramp antibodies - AT-TPO and AT-TG (at least 70-

80% of cases). Thus, the detection of classical anti-rampant carrotitel is inappropriate to distinguish the BG from chronic autoimmune, postpartum and nonsense ("silent") thyroiditis, but may, in the amount with other signs, to significantly help in the differential diagnosis of BG and functional autonomy (Fa) of the brush. It should be remembered that at-TPOs and AT-TGs can be found in healthy people without some kind of browsing diseases. Larger diagnostic value is the determination of the level of AT-RTTG.

Thyroidismantomantomotane - markers of diffuse toxic goiter. Sets for the definition of these autoantibodes by the method of enzyme immunoassay (ELISA) are available.

All autoantoantibodes towards TG receptors (including thyroidism and thyroid-blockingautantomantomotane) are determined by measuring the binding of IgG from the serum of patients with TSG receptors. These autoantibodies are detected at about 75% of patients with diffuse toxic goiter. The test for all autoantibodies to TSTH receptors is easier and cheaper than the test on thyroidismantomantomotane.

TREATMENT

First of all, planning treatment, it is necessary to clearly understand that with BG we are talking about an autoimmune disease, the cause of which is the production of antibodies to the RTTHIMMUNE system. Contrary to this, it is very often encountered with the idea that the surgical removal of the part of the pin (subtotal resection) in itself can cause the remission of the disease (that is, in essence of the autoimmune process). Although both the Surgery of BG and the therapy with the radiocyter is ideologically perceived only as the removal of autoimmune aggression from the organism of the target organism, liquidating thyrotoxicosis. Currently, there are three methods of treating BG, each of which has its own estate and disadvantages.

1. Conservative therapy

It is prescribed to achieve eutipereed for operational treatment, as well as in individual groups of patients, as a basic long course of treatment, which in some cases leads to a resistant. Long-term conservative therapy makes sense to plan far from all patients. First of all, we are talking about patients with a moderate increase in the volume of the threshold (up to 40 ml) without serious thyrotoxic complications. An important condition for the planning of long-term thirtotathicherapy is the readiness of the patient follow the recommendations of the doctor (compliance) and the availability of qualified endocrinological assistance. Conservative therapy is inappropriate to plan in patients with nodal formations in a

pin more than 1-1.5 cm, as well as in the presence of pronounced complications of thyrotoxicosis (atrial fibrillation, thyrotoxic myocardiodestrophia, which has pronounced blood circulation, osteoporosis, etc.). Practically meaningless and, most importantly, insecure for the patient, the appointment of repeated courses of conservative treatment in the development of a thyrotoxicosis recurrence after 12-24 plasticity therapy after 12-24.

As the main thyreostatics of many decades in clinical practice throughout the world, preparations from the group of thionamides are used: thiamazole (methisol, methimazole, tyrosol, mercazolyl) and propylthyoltioqil (vocational propitiation). The key mechanism of the actions of thionamide is that, falling into the threshold, they suppress the effect of thyroid peroxidase, inhibit the oxidation of iodine, the iodization of thyroglobulin and the condensation of uodtirosins. As a result, the synthesis of thyroid hormones is stopped and thyrotoxicosis is stopped. Staemazole reduces the main exchange, accelerates the removal of the thyroid gland of iodides, increases the reciprocal activation of the synthesis and the release of TTG hypophism. It does not affect the thyrotoxicosis, which developed due to the release of hormones after the destruction of the thyroid cell (with thyroid). Along with this, the hypothesis is put forward that thionamides/

The duration of the action once adopted dose of Tyrosol® is almost 24 hours, so the entire daily dose is prescribed to one reception or divided into two one-time doses. Tyrosol® is represented in two dosages - 10 mg and 5 mg of thiamazole in one tablet. The dosage of tyrosol® 10 mg allows you to reduce twice the number of tablets taken by the patient, and, accordingly, increase the level of patient compliance.

Propylthyouracil. Blocks thyroid-peroxidase and inhibits the transformation of ionized iodine into an active form (elementary iodine). Disrupts the iodization of Tyrozine residues of thyreoglobulin molecule with the formation of mono- and diodeodthyrosine and, further, tri- and tetraiodinyrine (thyroxine). The extractoreoid effect is in the braking of the peripheral transformation of tetraiodththththyous in triiodothyronine. Eliminates or weakens thyrotoxicosis. It has a zobogenic effect (increasing thyroid sizes), due to the increase in the secretion of the thyrotropic hormone of the pituitary gland in response to a decrease in the concentration of thyroid hormones in the blood. The average daily dosage of propylthiocila is 300-600 mg / day. The drug take fractionally, every 8 hours. PTU accumulates in the thyroid gland. It is shown that fractional reception of PTU is much more effective than a single daily dose. PTU has a less prolonged action than Tiamazole

The most adopted two modes of destination of thyaretics: constant titration of the dose of the drug appointed as a monotherapy ("block" scheme), and its purpose in a relatively larger dose in combination with thyroxine to maintain the eutyroid (block "block and replace"). The long-term results of treatment with both methods in terms of the probability of development of the resistivity of remission are the same, however, in the case of the "block and replacement" scheme, the maximum probability of remission is achieved after 6 months of therapy, while similar indicators for monotherapy in dose titration mode are achieved only after 18-24 months of treatment. At the beginning of the course of conservative therapy, including in the preparation of a patient to surgery, thionamides are prescribed in relatively large doses: 30-40 mg of thiamazole (for 2 receptions) or 300-400 mg of PTU (by 3-4 receptions). Against the background of such a therapy after 4-6 na, 90% of patients with the thyrotoxicosis of moderate severity, it is possible to achieve a eutheroid state, the first sign of which is the normalization of the level of SV. T4. The level of TSH may still remain reduced that it should not serve as a criterion for the lack of complete compensation for thyrotoxicosis in patients preparing for surgical treatment. For the period before the achievement of eutiperosis, and often for a longer period, most patients are advisable to appoint adrenobloclars.

When conducting conservative therapy after the normalization of the level of St. T4 patient is beginning to reduce the dose of thyaretics in about 2-3 weeks, they go to the receiving dose (10-15 mg per day). In parallel, starting from the moment of normalization of the level of St. T4, the patient is appointed leftotroxing dose of 50-150 μg per day. Such a scheme was called "blocked and notice." The thyaretics fully blocks the work of the pin, the levothyroxine replaces the formative deficiency of thyroid hormones (compensated by drug hypothyroidism). Scheme "Block and replace" easy use, since it allows you to completely block the products of thyroid hormones, which eliminates the possibility of recurrence of thyrotoxicosis. Criterion for adequacy therapy is the persistent maintenance of the normal level of St. T4 and TTG (the latter may come back for several months from the beginning of treatment). Contrary to the emerging ideas of thyaretics themselves do not have a "zobogenic" effect. An increase in the volume of the threshold against the background of their reception is naturally developed only with the development of drug hypothyroidism - the high level of TSH in this situation stimulates exclusively hyperplastic processes in the chart. Drug hypothyroidism can be easily compensated, assigning Levothyroxin within the framework of the "Block and Replacement" scheme.

Supporting therapy "Block and replace" - 10-15 mg of thiamazole and 50-150 μgleotocyne - no more than 24 months continues. Further increase in the volume of the threshold against the background of the conservative therapy, even subject to the persistent maintenance of the eutyroid, significantly reduces the chances of the treatment. After graduating course, drugs are canceled. Most often, recurrence develops during the first year after the cessation of therapy.

In general, thyreostatic therapy is sufficiently safe. Minor side effects, such as itching, urticaria, arthralgia, subfebilitation, felling, light disorders of taste and smell, usually transit and expressed very moderately; With their significant severity, you can transfer the patient to the reception of another drug. Throughout the patient, the patient with an interval of at least 1 time per month it is necessary to determine the level of leukocytes and blood platelets. Rare (0.06%), but a formidable complication of tionamide reception (both thiamazole, and with almost the same frequency, vocational schools) is agranulocytosis, causually rarely - isolated thrombocytopenia. Other extremely rare severe side effects include acute liver necrosis (PTU), cholesmune insulin syndrome with hypoglycemic states, lupus-like syndrome and vasculitis, which can be associated with antine-air cytoplasmic antibodies.

Beta adrenoblocators

Propranolol quickly improves the condition of patients, blocking beta-adrenoreceptors. Propranolol slightly reduces the level T3, braking the peripheral transformation T4 in T3. This effect of propranolol, apparently, is not mediated by the blockade of beta-adrenoreceptors. The usual dose of propranolol is 20-40 mg inside every 4-8 hours. The dose is selected so as to reduce the heart rate alone up to 70-90 minutes. As the symptoms of thyrotoxicosis disappear, the propranolol dose is reduced, and the drug is canceled upon reaching the eutiperosis.

Beta-adrenoblays eliminate tachycardia, sweating, tremor and anxiety. Therefore, the reception of beta-adrenoblockers makes it difficult to diagnose thyrotoxicosis.

Other beta adrenoblays are no more effective than propranolol. Selective beta1-adrenoblays (metoprolol) do not reduce the level T3.

Beta-adrenoblocators are especially shown in tachycardia even on the background of heart failure, provided that tachycardia is due to thyrotoxicosis, and heart failure - tachycardia. Relative contraindications to the use of propranolol - chronic obstructive pulmonary disease.

Iodida

A saturated solution of potassium potassium in a dose of 250 mg 2 times a day has a healing effect in most patients, but about 10 days, treatment is usually becoming ineffective (the "slipping" phenomenon). Potassium Iodide is used mainly to prepare patients with thyroid gland operations, since iodine causes the gland seal and reduces its blood supply. Potassium iodide is very rarely used as a means of choice with long-term treatment of thyrotoxicosis.

Therapy with radioactive iodine

It is possible without exaggeration to say, the most of the world most of the patients with BG, as well as with other forms of toxic goiter, are obtained as treatment with radioactive iodine. This is the relationship that the method is effective, not invasive, relatively cheap, deprived of those complications that can develop during an operation on the challenge. It was proved that, regardless of age, the risk of therapy 131i is significantly lower in operational treatment. The only contraindications to the treatment with radioactive iodine are pregnancy and breastfeeding, as it passes through the placenta, accumulates in the thyroid gland of the fetus (starting from the 10th week of pregnancy) and causes clutinism in a child. In significant quantities, 131i is accumulated only in the chart. After entering the gland, it begins to disintegrate with the release of β particles that have a mileage length of about 1-1.5 mm, which provides local radiation destruction of thyroidocytes. The safety of this treatment method demonstrates the fact that in a number of countries, for example, in the United States, therapy with radioactive iodine at BG is carried out in an outpatient basis. A significant advantage is that treatment 131i can be carried out without prior training by thionamides. Hypothyroidism is usually evolving within 6 mesprals of the introduction of radioactive iodine. Also, the benefits of the treatment with radioactive iodine include the cost (cheaper than in surgical treatment), the lack of restrictions for patients of advanced increase and with respect to the availability of any concomitant pathology, as well as the possibility of repetition of the procedure, if necessary.

Operational treatment

Absolute testimony for surgical treatment exist in the following groups of patients:

1. Patients with graves disease and suspicious or malignant clouds discovered in a thin game aspiration biopsy. According to some data, 10-20% of the closures in patients with graves disease are malignant.

2. Pregnant women who are poorly amenable to thyaretic therapy or who develop serious allergic reactions to medication treatment. The operation is usually done during the second trimester of pregnancy.

3. Patients who plan a pregnancy shortly after treatment, because Most doctors do not recommend to pregnant patients for at least 1 year after radio pooderapia.

4. Patients with compression symptoms. These symptoms usually do not pass after treatment with radioactive iodine.

5. Patients with Radiophobia.

Relative testimony for surgical treatment are:

1. The need to quickly eliminate thyrotoxicosis. After radioiodterepia, a latent period is noted with a duration of 6 weeks to 6 months, during which patients receive drug-based thyreostatic therapy, while surgery leads to rapid recovery.

2. Heavy flow of ophthalmopathy. Thyroidectomy stabilizes or reduces the manifestations of ophthalmopathy, while radioactive iodine tends to exacerbate its flow (if the conduct is not combined with the appointment of corticosteroids).

3. Significant increase in pin (more than 100 ml) with a relatively low absorption of radioactive iodine.

According to modern ideas, purposeful treatment, as well as the radioactive iodine discussed therapy discussed above, is the removal of the threshold, on the one hand, ensuring the development of postoperative hypothyroidism, and on the other, which is most importantly - excluding any possibility of tireotoxicosis recurrence. To this end, thyroidectomy is recommended with the obligatory allocation of returnable gangny nerves and the pancake glands. Conducting subtotal resections of the pin, on the one hand, the uncomfortable risk of preserving or distant recurrence of thyrotoxicosis, and on the other, does not exclude the development of hypothyroidism. In this connection, it is important to understand that the pathogenesis of thyrotoxicosis in grave disease is mainly due not to a large volume of the hyperfunctioning tissue of the thyroid gland (it may not be increased at all), and with circulation of stimulating thyroid gland antibodies that produced lymphocytes. Thus, when removing during surgery, the "target" is left for

antibodies for antibodies to the TTG receptor, which even after complete removal of the thyroid gland can continue to circulate in the patient throughout the patient.

Currently, postoperative hypothyroidism has ceased to be considered as a complication of operational treatment of BG, and is its goal. The prerequisite for this was the introduction into the wide clinical practice of modern synthetic drugs of Levothyroxin, thanks to which postoperative hypothyroidism is quite easily compensated and incurs to a decrease in the quality of life of patients. It should be noted that by itself postoperative hypothyroidism is actually not developing, since the patient immediately postoperative (on the 11th day) begins to obtain replacement therapy with levothyroxin drugs. Modern levothyroxin preparations allow you to maintain the quality of life in patients with hypothyroidism, which differs little from those in healthy people. Thus, the Levothyroxinaeutioks® drug is presented in the six most necessary dosages: 25, 50, 75, 100, 125 and 150 μg of Levothyroxin. A wide range of dosages allows you to simplify the selection of the required dose of Levothyroxin and avoid the need to crush the tablet to get the necessary dosage.

Thus, a high dosing accuracy is achieved and, as a result, the optimal level of hypothyroidism compensation. Also the lack of the need to crush the tablets makes it possible to increase the compliance of patients and the quality of their lives. This confirms not only clinical practice, but also the data of many studies, aimedly studied this issue. When the condition of daily reception of the replacement dose of Levothyroxin for the patient, there are practically no restrictions; Women can plan pregnancy and give birth, without fear of the development of thyrotoxicosis recurrence during pregnancy or (quite often) after childbirth. Obviously, in the past, when, in fact, approaches to the treatment of graves disease, meaning more economical resection of the thyroid gland, hypothyroidism was naturally considered as an unfavorable outcome of the operation, since the therapy of the thyroid gland extracts of animals (thyroidine) could not ensure proper compensation of hypothyroidism. It is possible without exaggeration to say that today there is no hypothyroidism, the compensation of which, with the competent use of modern levothyroxin preparations, would be impossible. The reasons for failures in compensation for postoperative hypothyroidism should be searched either in the insufficient qualifications of the doctor conducting replacement therapy, or in non-compliance with the patient, sufficiently simple recommendations on the drug reception.

Treatment of Graves Disease during pregnancy, Neonatal Greivsai Disease Breastfeeding

Taking into account the difficulties that arise in the treatment of diseasesgrius during pregnancy, the fact of its planning a woman with this disease can essentially can determine the choice of primary treatment. A radical cure or, at a minimum, more or less long-term remission after thyaretic therapy should be achieved before the occurrence of pregnancy, and the euthyroidism must be maintained up to delivery. Other problems are actually the treatment of graves disease during pregnancy, neonatal graves and breastfeeding disease.

If Graves's disease develops in time of pregnancy or if it comes to the development of pregnancy against the background of Greiva's disease, thyaretic drugs should be appointed in the minimum dose required to maintain the level of SV. T4 on the upper boundary of the norm or somewhat above the norm. The use of the "block and replacement" scheme during pregnancy is not shown, since thyaretics should be appointed in a larger dose, which carries the risk of the formation of goiter and hypothyroidism in the fetus. PTU is a preparation of the first choice for the treatment of thyrotoxicosis during pregnancy, since there is no data that it was combined with embryopathy. If a woman develops the intolerance to vocationally, it shows the purpose of carbymazole or thiamazole. If it is impossible to control thyrotoxicosis in the second trimester of pregnancy, operactive care can be taken. The real need for this may occur extremely rare, especially since the severity of thyrotoxicosis in its mass of graves is significantly and progressively reduced.

It is believed that neonatal illness develops in 0.1-0.2% of children born women with this disease. Specific symptoms in a newborn are usually absent, and their appearance may be delayed. The intrauterine thyrotoxicosis of the fetus can be suspected based on the lag in development, tachycardia. A larger prognostic value is the discovery of high-level APTTG women. The determination of the level of the ATRTTGV The third trimester of pregnancy is shown to women who, in order to maintain the eutyroid, received thyaretic therapy for pregnancy, as well as those women who are operated on about Graves' sickness or received treatment with radioactive iodine. In the last two cases, the APTTG products can continue long enough A larger prognostic value is the discovery of high-level APTTG women. The determination of the level of the ATRTTGV The third trimester of pregnancy is shown to women who, in order to maintain the eutyroid, received thyaretic therapy for pregnancy, as well as those women who are operated on about Graves' sickness or received treatment with radioactive iodine. In the last two cases, the APTTG products may continue long enough. The liquidation of thyrotoxicosis

after ablative therapy does not yet imply an immunological remission of graves disease, and producing antibodies can penetrate the placenta and stimulate the fruit. In practice, it is quite enough to determine the level of TBII, although the TSAB level would be more informative.

Breastfeeding during the reception of thyaretics is quite safe. Again, PTU theoretically has advantages over the thiamazole, since a lesser extent penetrates milk. Nevertheless, the risserness of the hypothyroidism in the child is impossible to completely fit. This situation shows the appointment of thyroidostatics in a minimum dose and periodic (every 2-4 week) Study of the child's imaging function. From a practical point of view, the temporary remission of Greiva's disease, which, as a rule, develops in the second half of pregnancy or, at least at its end, usually captures up to 3-6 months of the postpartum period, during which feeding is absolutely safe. After the last 6 months in modern conditions, only a small number of infants, maternal milk is the basis of nutrition. In this regard, more rational (compared to frequent control of the child's imagination) is the cessation of lactation or a daily appointment of a woman's adequate dose of thyaretics, which is solved individually.

FORECAST

BG is one of the most frequent autoimmune diseases of a person. Its clinical picture and forecast in most suitable are determined by persistent thyrotoxicosis, which, in the absence of adequate treatment, can lead to severely info. The most important principles of treating BG, although not devoid of deficiencies, but allow you to completely deliver the patient from thyrotoxicosis and ensure an acceptable quality of life.