**Hypophysis (pituitary gland) -** **Clinical laboratory diagnostics of adrenal gland -2**

 Biologically active substances synthesized in internal secretion glands, secreted into the blood and lymph, involved in the regulation of metabolism and physiological processes are called hormones. The thing that distinguishes hormones from other physiologically active substances is that they have specific properties depending on their chemical structure.

Disturbances in the functions of the internal secretion glands vary according to their causes and development mechanisms:

1. Violation of the central regulation of the function of the glands;

2. Pathological processes occurring in the glands themselves;

3. Extraglandular changes of hormone activity.

During infectious and inflammatory diseases of the central nervous system, tumor, trauma, etc., the function of the endocrine glands is disturbed. Damage or stimulation of the limbic system, reticular formation, midbrain decreases or increases the secretion of hormones. Diabetes, thyrotoxicosis, etc. stress and mental traumas play an important role in the pathogenesis of endocrinopathies.

 The central regulation of the functions of the endocrine glands is realized through the transhypophyseal and parahypophyseal pathways. Thyroid, gonadal, and adrenal cortex are regulated by the transhypophyseal pathway, which involves the hypothalamo-hypophysis-peripheral gland system. The transhypophyseal pathway is realized according to the principles of direct and feedback.

According to the principle of direct connection, under the influence of impulses from different departments of the central nervous system, the secretion of appropriate releasing hormones occurs from the neuro-secretory nuclei of the hypothalamus. In response to this, appropriate trophic hormones are secreted in the adenohypophysis. Effector hormones are produced in peripheral glands under the influence of tropic hormones.

The essence of the feedback principle is that the regulated parameter has the opposite effect on the operation of its regulator. For example. The concentration of thyroxine in the blood decreases the concentration of thyroliberin and TTH (thyrotropin hormone) respectively.

 **Indicators characterizing the somatotropic function of the hypophysis (STH)**

 Somatotropic hormone (STH) is a peptide of 191 amino acids secreted by the anterior lobe of the hypophysis gland. The daily dose of this hormone is 500 mcg. STH stimulates protein synthesis, mitotic division, accelerates lipolysis. Inactivation of the hormone in the blood is carried out by hydrolysis. Compared to other hormones, STH is secreted from the hypophysis gland in a small amount (5-15 µg of tissue). The main function of STH is to stimulate neck elongation in the body. STH stimulates the transport of amino acids into the cell in an insulin-dependent manner, ensuring protein synthesis. It also affects the uptake and oxidation of glucose by fat, muscle and liver tissue. STH increases the sensitivity of adipocytes to the lipolytic effect of catecholamines and decreases the sensitivity to the lipogenic effect of insulin. These effects cause fatty acids and glycerol to move from adipose tissue into the blood and be metabolized in the liver.

**The level of somatotropic hormone in the blood**

 **STH blood level is normally 0.4-10.0 ng/ml in male and 1-14 ng/ml in female.** The secretion of this hormone increases during physical load and deep sleep.

 STH stimulates cell growth directly, but also through insulin-like growth factor I and II (somatomedin).

STH is secreted unevenly throughout the day. During most of the day, the amount of this hormone in the blood is recorded at a low level. Therefore, special provocation tests are used. STH secretion is mainly regulated by hypothalamus-synthesized STRF (somatotropin-releasing factor), somatostatin, and insulin-like growth factor.

 An increase in the concentration of insulin-like growth factor I in the blood slows down the transcription of STH genes in the hypophysis gland through feedback.

The main changes in the somatotropic function of the hypophysis gland are related to the increase and decrease of the hormone. Gigantism and acromegaly develop as a result of chronic hyperproduction of STH from the somatotroph cells of the anterior part of the hypophysis gland. Hyperproduction of STH in the period of osteogenesis before the closure of the epiphysis results in gigantism, in very few cases, it is found at young ages. In the period after closure of the pineal gland, hyperproduction of STH leads to acromegaly, it is found at the age of 30-50.

 Hypophysis dwarfism develops as a result of deficiency or complete loss of function of the anterior part of the hypophysis gland. STH deficiency is most often associated with type I damage to the hypothalamus. In particular, in some congenital forms of dwarfism, the synthesis and secretion of STH is not disturbed. In particular, although all the signs of hypopituitarism are manifested during **Laron's syndrome** in children, in contrast to the decreased concentration of insulin-like growth factor I in the blood, an increase in STH is observed. The main defect here is the disappearance of the ability of STH to stimulate insulin-like growth factor I.

 **Insulin-like growth factor I in the blood (Somatomedin)**

 The main factor in the concentration of insulin-like growth factor I in the blood is age. This factor starts from very low indicators in newborns (20-60 ng/ml) and rises to maximum numbers during puberty (600-1100 ng/ml).

The concentration of insulin-like growth factor I in the blood varies depending on STH and T4 hormone. A low concentration of insulin-like growth factor I is found in severe forms of T4 deficiency. Replacement therapy with sodium-levothyroxine leads to an increase in the concentration of insulin-like growth factor I in the blood to normal. Another factor that ensures the concentration of insulin-like growth factor I is nutrition. In children and adults, meeting the protein-energy supply of the body in accordance with the demand is an important condition for ensuring the normal concentration of insulin-like growth factor I. Although the concentration of insulin-like growth factor I in the blood of children with acute protein deficiency decreases, it normalizes after proper nutrition. Liver failure, inflammatory diseases of the intestines, and kidney failure also cause a decrease in the concentration of insulin-like growth factor I in the blood.

 In clinical practice, insulin-like growth factor I plays an important role in evaluating the function of the hypophysis gland. Because the concentration of insulin-like growth factor I is always high in patients with acromegaly, the assessment of this hormone is considered more important than STH. In patients with acromegaly, the concentration of insulin-like growth factor I is approximately 7 times higher than the normal level. In such patients, the concentration of insulin-like growth factor I is correlated with the severity of the disease and the growth of soft tissues.

To confirm the completion of the treatment of patients with acromegaly, the following laboratory indicators are taken as a basis:

- The level of STH in the blood on an empty stomach is lower than 5 ng/ml;

- After hormone therapy, the level of STH in the blood is lower than 2 ng/ml;

- The concentration of insulin-like growth factor I in the blood is within normal limits

 **Adrenocorticotropic hormone (ACTH) in blood plasma**

The level of ACTH in blood plasma consists normal as < 22 pmmol/l at 8:00 am and <6 pmmol/l at 10:00 pm.

ACTH - adrenocorticotropic hormone consists of 39 amino acids, and mainly controls the synthesis and secretion of hormones of the adrenal cortex - cortisol, cortisone, corticosterone. In addition, the secretion of progesterone, estrogen and androgens also increases. Also, the effect of ACTH and its components on memory motivation and acquisition processes has been proven.

Excretion of ACTH into the blood occurs with a daily rhythm, the maximum concentration is recorded at 6 am, and the minimum concentration is recorded at 10 pm. Stress is considered a strong stimulator of this hormone.

Itsenko-Cushing’s disease is characterized by an increase in the level of both ACTH and cortisol and 17-OKS (oxyketosteroids) in the blood. It is important to determine the level of ACTH in the differential diagnosis of Itsenko-Cushing’s disease and various forms of Cushing's syndrome. **A decrease in ACTH secretion is noted in patients diagnosed with corticosteroma and adrenal gland cancer. The level of this hormone in the blood increases in patients with Itsenko-Cushing’s disease and ectopic ACTH syndrome (pathological secretion of ACTH during a tumor of the bronchi or thymus gland).**

 Corticotropin-releasing hormone (CRH) test is used in the differential diagnosis of Itsenko-Cushing’s and ectopic ACTH syndrome. Thus, in the case of Itsenko-Cushing’s disease, the injection of CRH leads to a significant increase in ACTH secretion, while in non-hypophysis localized tumors that secrete ACTH, the level of ACTH does not change because there are not receptors against CRH.

 An increase in the level of ACTH in the blood occurs during cancer of the thyroid gland and thymus, ovaries and mammary gland and cancer of the stomach and large intestine. Diagnostically, in ACTH-ectopic syndrome, the level of ACTH in the blood is more than 44 pmmol/l and it is clinically important to study the level of the hormone in different veins.

In the case of primary deficiency of the adrenal cortex substance, the level of ACTH in the blood increases 2-3 times, that is, significantly. ACTH secretion accelerates both in the morning and in the evening. A CRH test is performed to assess the residual ACTH volume. In the case of hypophysis deficiency, the test with CRH does not react.

When the pathology is in the hypothalamus, the response of ACTH and cortisol to the corticotropin-releasing hormone (CRH) test is delayed.

**The level of Thyrotropin hormone (TTH) in the blood**

TTH level in newborns is normally 3-20 mME\l, in adults 0.2-3.2 mE\l.

Thyrotropin hormone (TTH) is a glycoprotein secreted by the adenohypophysis, which mainly stimulates the synthesis of thyroxine, triiodothyronine and secretion from the thyroid gland. In hypothyroidism, the TTH level increases. At this time, the decrease in the concentration of free T4 and T3 in the blood, and within the normal range in subclinical mild hypothyroidism, confirms the diagnosis. A low level of TTH in hypothyroidism indicates hypophysis or hypothalamic dysfunction and rules out thyroid dysfunction.

Table 10.9

Changes in the concentration of TTH during various diseases and conditions

|  |  |
| --- | --- |
| **Increase of Consistence**  | **Decrease of Consistence**  |
| I hypofunction of the thyroid gland | I hyperfunction of the thyroid gland |
| Subacute thyroiditis | Hypothalamic-hypophysis insufficiency |
| Hashimoto's thyroiditis | Hypophysis tumors |
| Hypophysis tumors | Hypophysis trauma |
| **Ectopic tumors of lungs, mammary gland** | Postnatal necrosis of the hypophysis gland |
| **Endemic goitre** | Taking thyroid hormones |
| Inflammation of the thyroid gland | Itsenko-Cushing’s syndrome |
| Condition after iodine therapy | Taking aspirin, heparin, corticosteroids |
| Thyroid cancer |  |

 In patients with hypothyroidism, the concentration of TTH is of great importance in the determination of thyroxine replacement therapy. The dose of L-thyroxine can be determined by determining the concentration of TTH.

 In hyperthyroidism, TTH synthesis and secretion slows down.

**Indicators characterizing reproductive function**

The reproductive system consists of certain structures of the hypothalamus and hypophysis and target cells /codocyte/ (fallopian tubes, uterus, etc.). The elements of the reproductive system interact with information signals that allow them to function in a complete way.

Studying the level of reproductive system hormones plays an important role in discovering the causes of male and female infertility based on hormonal regulation disorders.

Classification of hormones that regulate reproductive function:

- Hypothalamus: Gonadotropin releasing hormone, Prolactin RH, GRIQ, PRIQ

- Hypophysis: Luteinizing (LH), Follicle stimulating (FSH), prolactin

Ovaries: estrogen, gestagen, androgen, inhibin

Placenta: estrogen, gestagen, chorionic hormone, prolactin

Seminiferous tubules: androgen, inhibin

Adrenal gland substance: androgens, estrogens

 Together with FSH, luteinizing hormone affects the reproductive function of the body. In women, this hormone ensures the secretion of estrogen from the ovaries, participates in the completion of the ovulation process. In the male body, it affects the Leydig cells that synthesize testosterone. Luteinizing hormone stimulates the synthesis and activity of T3 T4 hormones, which ensure growth by acting on the receptors of the epithelial cells of the thyroid gland.

 **Follicle stimulating hormone (FSH)**

Follicle-stimulating hormone (FSH) is secreted from the anterior lobe of the hypophysis gland and regulates follicle maturation and ovulation readiness in women. In men, this hormone ensures the development and function of seminiferous tubules and seminiferous tubules, and the process of spermatogenesis in Sertoli cells.

 Table 10. 16

|  |  |
| --- | --- |
| Level  |  FSH Ed/l |
| Female: |  |
| Follicular phase | 4-10 |
| Ovulation phase | 10-25 |
| Lutein phase | 2-8 |
| Menopause phase | 18-150 |
| Male | 2-10 |
|  |  |
| **Increase of Consistence**  | **Decrease of Consistence**  |
| Seminoma | I hypofunction of the hypophysis  |
| Menopause due to dysfunction of the ovaries | Taking estrogen, progesterone, phenothiazine |
| Gonadotropin hypofunction |  |
| - Klinefelter's syndrome |  |
| - Shereshevsky-Turner syndrome |  |
| - Castration |  |
| -Ectopic tumors |  |
| -Initial phase of hypophysis hyperfunction |  |
| Taking clomiphene, levadopa |  |
|  |  |

**Prolactin in blood serum**

The normal level of prolactin in the blood is 61-512 mME/l in female and 58-475 mME/l in male.

 Prolactin is synthesized in the lactogenic cells of the anterior lobe of the hypophysis. Its synthesis and secretion are carried out under the stimulating-inhibiting influence of the hypothalamus. In addition to the hypophysis, the decidual membrane (because amniotic fluid contains prolactin) and the endometrium also synthesize prolactin. Together with estradiol, prolactin in female affects the growth and function of the mammary glands, causing lactation. The role of this hormone in male is unknown.

 Dopamine has a retarding effect on prolactin secretion. In addition to dopamine, noradrenaline, acetylcholine, and gamma-amino fatty acid also have a delaying effect on prolactin secretion.

 Tryptophan derivatives serotonin and melatonin play the role of prolactin-releasing factor and stimulate hormone secretion. The concentration of prolactin in the blood increases during sleep, physical activity, hypoglycemia, lactation, pregnancy, stress.

**Macroprolactin**

Normally, macroprolactin is 0-10% of total prolactin.

Since macroprolactin does not have biological activity, its excess amount in the blood - macroprolactinemia is not accompanied by clinical symptoms and it’s a laboratory diagnostic phenomenon that does not require treatment. A macroprolactin level of more than 30% in the blood gives reason to talk about macroprolactinemia. The following are taken as the basis for the macroprolactin test:

- After the precipitation of immune complexes, the result of the level of prolactin in the blood is up to 40% of the initial indicator

- After the precipitation of immune complexes, the result of the level of prolactin in the blood is up to 60% of the initial indicator

- After the precipitation of immune complexes, the result of the level of prolactin in the blood is up to 40%-60% of the initial indicator

**Hypothalamus- hypophysis - indicators characterizing the adrenal gland system**

The anterior lobe of the hypothalamus hypophysis and the cortex of the adrenal gland are functionally united in the hypothalamus-hypophysis-adrenal gland system.

 The adrenal gland is composed of a shell and a brain substance that perform various functions. Histologically, the cortical substance consists of 3 layers - peripheral glomerular, middle layer and the lowest reticular layer. Only aldosterone is secreted from the glomerulus. The other two layered and reticular layers form a functional complex and secrete the main hormones of the adrenal cortex (glucocortoids and androgens).

 In the stratum corneum of the adrenal gland, pregnenolone synthesized from cholesterol is converted to **17 α-oxypregnenolone, which serves as the primary substrate for cortisol, androgens, and estrogens.** 17 α-oxypregnenolone produces 17 α-oxyprogesterone, which is hydroxylated and converted to cortisol. The secretory products of the stratum corneum and reticularis are called steroids and have androgenetic activity. Dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEAS), androstenedione, and testosterone are derived from 17 α-oxypregnenolone.

 The hormones of the adrenal cortex (glucocortoids and androgens) are regulated by the hypothalamus-hypophysis system. Corticoliberin, synthesized in the hypothalamus, comes to the anterior part of the hypophysis through the portal veins and causes the synthesis of ACTH. Under the influence of ACTH, the side chains of cholesterol are broken, which slows down the steroidogenesis process in the cortex of the adrenal gland, which interacts with the corticoliberin-ACTH-free cortisol chain, as well as the increase in the level of free cortisol in the blood causes a delay in the level of corticoliberin through a feedback mechanism.

Diseases of the cortex of the adrenal gland manifest themselves in the form of hyperfunction or hypofunction. During some pathologies, the increase of one hormone leads to a decrease in the other, which belongs to the dysfunction group.

The following syndromes are distinguished during diseases of the adrenal cortex:

- Hypercorticism:

- Itsenko-Cushing’s disease (hypothalamus-hypophysis disease);

- Cushing's syndrome - corticosteroma (malignant or benign) or bilateral small-nodular dysplasia of the cortex substance of the adrenal gland;

- ACTH-ectopic syndrome: tumors of bronchi, pancreas, thymus, liver, ovaries secreting ACTH or corticotropin-releasing hormone;

- Feminization and virilization (synthesis of estrogen or androgens)

- Hypocorticism:

- Primary

- Secondary

- Tertiary

- Dysfunction of the adrenal cortex

Adrenogenital syndrome (AGS)

 **The following indicators are used to study the functional state of the hypothalamo-hypophysis-adrenal system:**

- For assessing the function of glucocorticoids - cortisol, ACTH, and 17- hydroxyprogesterone (- 17-OHP)

- For assessing the function of mineralocorticoids - aldosterone, plasmin renin activity (PRF)

 For assessing androgen function - testosterone, dehydroepiandrosterone (DHEA), dehydroepiandrosterone-sulfate (DHEAS), androstenedione (A4)

**Cortisol in the blood**

The concentration of free cortisol in the blood is normally at 8.00-200-700 nmol/l, at 20.00 55-250 nmol/l. The difference between morning and evening concentrations should be more than 100 nmol/l. During adrenal insufficiency, the level of cortisol in the blood decreases. During adrenal gland deficiency I and II, the amount of cortisol, free cortisol, 17-oxycorticosteroid (17-OKS) in urine also decreases. In non-acute adrenal insufficiency, the concentration of cortisol in the blood Should not decrease due to the weakening of the metabolism of the hormone. In such doubtful cases, functional tests are performed with ACTH preparations. These include a single intramuscular injection of corticotropin and an intravenous injection of synactin. In healthy people, the level of cortisol increases more than 2 times after conducting these calculations. Absence of reaction to the injection of preparations into the body indicates the presence of I deficiency of the adrenal gland.

Adrenal gland response to ACTH injection is preserved during type II adrenal insufficiency. However, long-term adrenal insufficiency leads to atrophy of the adrenal medulla, in which it loses its ability to increase glucocorticoid secretion against ACTH administration.

 An increase in the concentration of cortisol in the blood is observed during Itsenko-Cushing's disease and Cushing's syndrome. During Itsenko-Cushing's disease, the level of cortisol in the blood usually increases, but the daily level of the hormone undergoes changes at different hours. At 8.00 in the morning and at 20.00 in the evening are considered the main indicators. In some Itsenko-Cushing's patients, the concentration of cortisol in the blood can remain normal due to the weakening of the metabolism of the hormone. In this case, dexamethasone tests are used. A decrease in the level of cortisol by 2 times or more after the test eliminates the diagnosis of Itsenko-Cushing's disease. On the contrary, failure to observe a delay in cortisol secretion (50% or more) confirms the diagnosis of the disease.

ACTH-ectopic syndrome is characterized by a significant acceleration of cortisol secretion compared to other forms of hypercortisolism. Thus, if the rate of cortisol secretion during Itsenko-Cushing's disease is 100 mg/day, it is equal to 200-300 mg/day in patients with ACTH-ectopic syndrome.

 Cortisol blood levels may be elevated in emotional individuals.

 The concentration of cortisol in the blood can increase in Cushing's syndrome, hypothyroidism, cirrhosis of the liver, terminal conditions, decompensated diabetes, asthmatic conditions and intoxication in non-drinkers.

 An excess of cortisol in the blood, which goes with maintaining the daily rhythm, is observed during stress, pain, fever and during Cushing's syndrome. Acute infections, meningitis, brain tumors, acromegaly, right ventricular failure, liver failure, renal hypertension, hypophysis hyperfunction, mental depression, taking synthetic analogs of glucocorticoids (prednisone, prednisolone), amphemin, estrogen concentration in the blood also increases. A decrease in the concentration of cortisol in the blood is detected in the case of type I deficiency of the adrenal gland, Addison's disease, hypophysis.

**Free cortisol in urine**

 **The concentration of free cortisol in urine is normally 30-300 nmol/l or 15-30 nmol/l daily creatinine.** Cortisol that is not bound to blood plasma proteins (free) is filtered from the renal glomeruli and excreted in the urine. Free cortisol in blood plasma is one of the main biologically active forms of the hormone. The concentration of free cortisol in the daily urine directly reflects the level of free cortisol in the blood. The determination of the level of free cortisol in the daily urine is the main test for the diagnosis of adrenal gland hyperfunction. When evaluating this test, it is necessary to take into account that the concentration of the hormone will increase during physical load in obese patients.

 The level of free cortisol in the urine of patients with renal failure is reduced and does not reflect the measures of cortisol secretion. Most patients with Itsenko-Cushing’s syndrome have an increased level of free cortisol in their urine. A very high level of free cortisol in the urine confirms the diagnosis of carcinoma of the adrenal gland.

In cases of adrenal cortex I and II insufficiency, the concentration of cortisol in the blood and the level of free cortisol, 17-oxyketosteroid (17-OKS) in the urine are determined. In adrenal insufficiency type II, the excretion of free cortisol and 17-oxyketosteroid (17-OKS) may not increase in the first days after stimulation with synacten. But in the next 3-5 days, the level of these hormones in the urine should be compared with healthy people.

In complete adrenal insufficiency type I, the level of free cortisol and 17-oxyketosteroid (17-OKS) does not change after stimulation, but in incomplete adrenal insufficiency, the level of free cortisol and 17-oxyketosteroid (17-OKS) in urine decreases, after stimulation on the first day, it can increase 3-5 times even in healthy people. In recent years, a directed-phase high-performance liquid chromatography method has been developed for the estimation of the level of corizone and excretion of corizone.

**17-oxyketosteroids in urine**

**The concentration of 17-oxyketosteroids (17-OKS) in urine is normally 5.2-13.2 μmol/day.**

17-oxyketosteroids are metabolites of steroid hormones, cortisol (F), cortisone (E) 11-deoxycortisol (S), tetrahydrocortisol (THF), tetrahydrocortisone (THE) tetrahydro-11-deoxycortisol (THS).

 The main component of urinary 17-oxyketosteroids are tetrahydrometabolites of cortisol. It should be noted that the daily urinary excretion of 17-oxyketosteroids is not diagnostically significant as it depends on the patient's weight and other factors.

Urinary excretion of 17-oxyketosteroids is reduced in chronic adrenal insufficiency. In suspicious cases, a test with ACTH preparations is carried out. Excretion of 17-oxyketosteroids by 1.5 times or more on the first day after ACTH injection, and even more on the 3rd day, indicates the reserve function of the adrenal cortex, and the diagnosis of adrenal cortex I deficiency is denied.

Increased urinary excretion of 17-oxyketosteroids is observed in Itsenko-Cushing's disease, Cushing's syndrome, alimentary-constitutional and hypothalamo-hypophysis obesity. Liddle's dexamethasone test is performed for the differential diagnosis of Itsenko-Cushing's disease and obesity. A decrease in urinary excretion of 17-oxyketosteroids by 50% more than the norm is considered against Itsenko-Cushing's disease. At this time, the level of 17-oxyketosteroids excreted in urine should not exceed 10 μmol/day. If the urinary excretion of 17-oxyketosteroids is reduced by more than 2 times, the diagnosis of Itsenko-Cushing's disease or Cushing's syndrome can be made. A large dexamethasone test is used to differentiate between the diagnoses of Itsenko-Cushing's disease or Cushing's syndrome. A delay of 50% or more of 17-oxyketosteroids indicates Itsenko-Cushing's disease, and the absence of a delay indicates Cushing's syndrome.

 **Urinary 17-ketosteroids (17-KS)**

**17-ketosteroids (17-KS) in urine are normal: female 20-40 years old: 5-14 mg/day, male: 20-40 years old 9-17 mg/day, after 40 years of age, a decrease in 17-KS excretion is observed.**

Urinary 17-ketosteroids (17-KS) are metabolites of androgens secreted from the retina of the adrenal gland and the gonads. Only a small part of the 17-ketosteroids excreted in the urine (17-KS) originates from the precursors of glucocorticoids. **Evaluation of 17-ketosteroids in urine (17-KS) serves to evaluate the functional activity of the adrenal cortex**. A decrease in 17-ketosteroids excreted in urine is observed in chronic insufficiency of the adrenal cortex, and its increase is observed in androsteroma, Itsenko-Cushing's disease or Cushing's syndrome, in congenital hyperplasia of the adrenal cortex.

For congenital hyperplasia of the cortex substance of the adrenal gland, it is important to note the increase in the excretion of 17-ketosteroids in the urine, as well as the increase in the ACTH activity of the plasma, the lower limit of the normal concentration of cortisol in the blood and 17-oxyketosteroids in the urine. Since the drugs used in the treatment of Cushing's disease slow down the synthesis of glucocorticoids (17-KS), the dynamic study is not recommended in terms of evaluating the effectiveness of the treatment.

**Dehydroepiandrosterone (DHEA), dehydroepiandrosterone-sulfate (DHEA-sulfate), ∆4-androstenedione ( A4 )**

An increase in these hormones, along with signs of hyperandrogenism, indicates that androgen excess is of adrenal gland origin ( congenital hyperplasia of the adrenal cortex ) . According to some authors, **an increase** in DHEA and A4 in the blood is observed both in the deleted form of congenital hyperplasia of the adrenal cortex substance and in polycystic ovary syndrome, which makes it difficult to differentiate hyperandrogenism of adrenal gland and ovarian origin.

 Dehydroepiandrosterone (DHEA), dehydroepiandrosterone-sulfate (DHEA-sulfate), ∆4 - androstenedione ( A4 ) and total and free testosterone levels are determined to determine the cause of hypersecretion of androgens during hyperandrogenism.

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An increase in these hormones, along with signs of hyperandrogenism, indicates that androgen excess is of adrenal gland origin (congenital hyperplasia of the adrenal cortex). According to some authors, **an increase** in DHEA and A4 in the blood is observed both in the deleted form of congenital hyperplasia of the adrenal cortex substance and in polycystic ovary syndrome, which makes it difficult to differentiate hyperandrogenism of adrenal gland and ovarian origin.

 Dehydroepiandrosterone (DHEA), dehydroepiandrosterone-sulfate (DHEA - sulfate), ∆4-androstenedione (A4), and total and free testosterone levels are determined to determine the cause of hypersecretion of androgens during hyperandrogenism.

 **Large dexamethasone test** (test with 8 mg of dexamethasone, **Liddle's large** **test**) when a **small dexamethasone test** is negative, it is performed to determine the exact form of pathological hypercorticism, i.e. for the differential diagnosis of Itsenko-Cushing's disease and Cushing's syndrome. After examining the baseline level of cortisol, ACTH and urine 17-oxycorticosteroid (17-OKS), patients are prescribed **dexamethasone** orally for 3 days (daily dose of 8 mg). Urine 17-oxycorticosteroid (17-OKS) is taken again on the 3rd day of taking the drug. The level of cortisol and ACTH in the blood is determined at 8 o'clock in the morning on the 4th day of taking dexamethasone.

 Administration of 8 mg of dexamethasone causes suppression of cortisol and ACTH concentration by 50% or more in patients diagnosed with hypophysis hypercortisolism, as Itsenko-Cushing's disease patient.

 This result reflects that the main problem lies in the anomaly of the hypothalamo-hypophysis-adrenal gland system chain, which goes with maintaining the feedback mechanism. The adrenal form of hypercortisolism, i.e. Cushing's syndrome, is characterized by a decrease in the level of ACTH, an increase in the level of cortisol and 17-OKS excreted in the urine. Absence of delay in the level of all three indicators (ACTH, cortisol, 17-oxyketosteroid) is characteristic for ectopic ACTH secretion syndrome.

 A paradoxical reaction may occur in adrenal medullary cancer (increased levels of cortisol and 17-OKS after the test)

**Abbreviated small dexamethasone test**. After taking 1 mg of dexamethasone at 11:00 p.m. on the same day, blood is taken again to determine the level of cortisol at 8:00 a.m. the next day.

 Cortisol levels in the blood of obese patients with pink striae decrease by 50% or more. In other pathologies of hypercorticism, a decrease in the level of cortisol in the blood is not observed.

**Abbreviated large dexamethasone test.** It is performed as a shortened mini dexamethasone test, only the patient takes 8 mg of dexamethasone at 11 o'clock in the evening instead of 1 mg.

The results are obtained as in the large dexamethasone test. Although abbreviated tests are less labor intensive, they do not have high specificity. Thus, obesity, depression, and the absence of suppression in patients receiving estrogen are falsely reported.

**ACTH stimulation test during adrenal gland insufficiency**. It allows to detect the hidden form of adrenal gland insufficiency, to carry out differential diagnosis between adrenal gland insufficiency I and II insufficiency. At present, ACTH synthetic analogue "Synacthen" or its prologized form " Synacthen -depot" is used for the test.

**A short trial with " Synacthen** ". It is performed to evaluate the reserve function of the adrenal gland.

In another group of patients, non-congenital 21-hydroxylase enzyme deficiency causes an increase in 17-OHP in the blood. In such patients, observing the increase of 17-OHP in the blood against ACTH injection is considered a characteristic test. To detect the hormonal activity of the adrenal glands, the following tests should be performed:

 Background levels of hormones

- Excretion of free cortisol (UFF) and free cortisol (UFE) in urine

 Directed-phase high-performance liquid chromatography of blood corticosteroids (cortisol, cortisone, corticosterone. 11-deoxycorticosterone, 11-deoxycorticosterol)

 -Determination of ACTH and cortisol in blood at 9.00 and 21.00, study of aldosterone level

- Study of plasma renin activity ( **PRF** ).

Study of androgens ( DHEA - C, A4-, testosterone )

- 17 - hydroxyprogesterone

**Congenital hyperplasia of the adrenal cortex with a defect of 21-hydroxylase** is diagnosed based on the clinical signs of Viral syndrome, with a blood level of 17-OHP exceeding 5 mg/ml in the early follicular phase of the menstrual cycle.

Studying the level of 11-deoxycorticosterone (DOC), 11-deoxycortisol (S), which are substrates of 11 β-hydroxylase, **plays a major role in the laboratory diagnosis of the form of congenital hyperplasia of the adrenal gland with a deficiency of 11 β-hydroxylase.** Information about these hormones in the blood can be obtained by the **method of doing high performance liquid chromatography** of corticosteroids.

**The level of estradiol in the blood**

The main representative of estrogens is estradiol, which has the highest biological activity. Estrone is obtained from estradiol in an enzymatic way, and its biological activity is not high and its level increases during pregnancy. At this time, estrone is synthesized from dehydroepiandrosterone-sulfate formed in the adrenal cortex of the fetus. Thus, estrone is an indicator that characterizes the state of the fetus. In the female body, estradiol is produced in the ovaries, granulosa cells and membrane of the follicles. After the beginning of pregnancy, the synthesis of estrogen is carried out massively by the couple. Adrenal gland and peripheral sebaceous glands are other organs where estrogen synthesis is carried out. Determination of estradiol concentration is important in evaluating the function of the ovaries (by aromatizing androgens). There is no exact information about the secretion of estrogen in the male body. The target organs of estrogen are uterus, uterus, vulva, fallopian tubes and mammary glands.

 These hormones ensure the development of secondary sexual characteristics in the body, physical and mental characteristics specific to female. Estrogens cause the cervical epiphyseal points to close.

**Progesterone in the blood**

It is a female steroid hormone, being synthesized by the corpus luteum, it promotes the proliferation of the mucous membrane of the uterus and the implantation of the fertilized egg into the uterus more easily.

 The concentration of progesterone is determined during the menstrual cycle to check whether ovulation has occurred or not. For the physiological effect of progesterone to be revealed, the previous effect of estrogen is important. The main target organ of the hormone is the uterus. The hormone induces a secretory transformation of the proliferative thickened endometrium, preparing it for implantation of the impregnated ovum. Also, progesterone gonadotropin stimulates the heat center by performing a control function in the gonadal system. This causes a 0.5°C rise in body temperature during the luteal phase of the menstrual cycle after ovulation. At the end of the menstrual cycle, the concentration of progesterone decreases and this leads to menstrual bleeding.

**Testosterone in the blood**

• Testosterone is an androgen hormone, which ensures the emergence of secondary sexual characteristics in men. The main source of testosterone is the Leydig cells of the seminiferous tubules. Testosterone stimulates spermatogenesis, the growth and function of the gonads, and ensures the development of the genitals and testicles. In particular, it has an anabolic effect on bones and muscles. Testosterone stimulates erythropoiesis by directly affecting the bone marrow and activating the synthesis of erythropoietin in the kidneys. Testosterone provides libido and potency. Testosterone synthesis is regulated by luteinizing hormone secreted from the hypophysis gland. It is the only hormone that ensures sexual maturity in male. Blood concentration increases after physical activity. Since the determination of free testosterone does not depend on the concentration of steroid-binding globulin (SBG), there is an indication for the determination of this hormone in diseases accompanied by an increase in SBG (hyperthyroidism, hyperestrogenia, pregnancy, taking oral contraceptives, etc.) or a decrease (hypothyroidism, obesity).

**LABORATORY DIAGNOSTICS OF THE THYROID GLAND**

 The thyroid gland is a single organ located in the front of the neck under the larynx. It is similar in structure to a shield and consists of a large number of small sacks i.e. that is, follicles, which are considered as the functional unit of the gland.

 **Features of impact of the thyroid hormones**

 *Differentiation and morphogenetic effect (influence on growth and development)*. The thyroid hormones ensure the normal development of the brain, nerves, connective tissue, reproductive and endocrine systems during embryonic development, as well as in children, and the optimal concentration of T3 and T4 in adults ensures normal mental activity.

 *Calorigenic (heat-generating) effect and participation in thermoregulation.* Under the influence of thyroid hormones, on the one hand, due to the oxidation of carbohydrates and lipids, the formation of ATA (adenosine triphosphatic acid) in the mitochondria is accelerated, on the other hand, the hydrolysis of ATA increases as a result of the increase in the activity of the Na+, K+-ATF-phase. As a result, additional energy is generated in the form of heat.

 *Involvement in protein metabolism.* Thyroid hormones ensure the normal catabolism of proteins.

 *Involvement in fat metabolism.* Thyroid hormones increase the breakdown of lipids and the mobilization of lipids from adipose tissue.

 *Thyroid hormones increase the sensitivity of β-adrenergic receptors* to adrenaline and their expression on the cell membrane (for example, in myocardial cells).

 An excess of thyroid hormones leads to hyperthyroidism and a deficiency causes hypothyroidism. Hyper- and hypothyroidism express in a number of symptoms (Table 1).

Table 1.

Sign of hyper- and hypothyroidism.

|  |  |  |
| --- | --- | --- |
| Organ, tissue and system  | Hypothyroidism | Hyperthyroidism  |
| 1 | 2 | 3 |
| In the entire organism level | Decreased protein synthesis affects growth (stunting)Reduction of metabolic processes, basic exchange and body temperatureHypercholesterolemiaDry, thick skin | Acceleration of protein catabolism and negative nitrogen balanceAn increase in basic exchange and body temperatureHypocholesterolemiaExophthalmos, moist skin |
| CNS | Mental retardation in children (cretinism)Drowsiness, lethargy, sluggishness, apathySensitivity to coldAn increase in the duration of reflexes | Acceleration of mental processesInsomnia, wakefulness, anxiety, agitationSensitivity to heatShortening of reflexes |
| Cardiovascular system | A decrease in the minute volume of blood, heart failure, bradycardia, arterial hypotension | Increased minute volume of blood, tachycardia.An increase in systolic blood pressure as a result of an increase in the work of the heart - secondary arterial hypertension |
| Digestive system | Decreased food intakeConstipationDecreased absorption of glucose | Increased food intakeDiarrheaIncreased absorption of glucose |

|  |  |  |
| --- | --- | --- |
| 1 | 2 | 3 |
| Skeletal muscle | Weakness, hypotonia | Weakness, tremor, decrease in muscle mass due to increased protein catabolism |
| Immune system | Development of immunodeficiency conditions, weakening of resistance to infectious diseases | Development of immunodeficiency conditions, weakening of resistance to infectious diseases (due to acceleration of protein catabolism) |
| Adipose tissue | Obesity due to reduced energy loss | Fat tissue volume reduction, weight loss |
| β-adrenoreceptors | A decrease in their number on the surface of cellsDecreased sensitivity to adrenaline | An increase in their number on the surface of cellsIncreased sensitivity to adrenaline |
| Enzymes | Decrease of activeness of the mitochondrial oxidative enzymes, Na+, К+- adenosinetriphosphatase, nicotinamide-adenine dinucleotide phosphate malate dehydrogenase, α-glucose phosphate dehydrogenase, etc.  | Decrease of activeness of the mitochondrial oxidative enzymes, Na+, К+- adenosinetriphosphatase, nicotinamide-adenine dinucleotide phosphate malate dehydrogenase, α-glucose phosphate dehydrogenase, etc. |

**Laboratory diagnosis of thyroid gland diseases**

The determination of thyroid function usually includes the following 4 tests:

* *Total thyroxine* (T4) – determination of serum thyroxine concentration. This includes protein-bound inactive thyroxine and free active thyroxine;
* *Free thyroxine* (FT4) – determination of free (biologically active) thyroxine concentration in serum;
* *Total triiodothyronine* (T3) – determination of total triiodothyronine concentration in serum. It consists of protein-bound (inactive) and free (active) triiodothyronine;
* *Thyroid-stimulating hormone* (TSH) – determination of serum concentration of TSH, a pituitary hormone.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|    AGE |        tth (mkme/ml) |  Т4 GENERAL (nmol/l) | Т4 FREE.  (pmol/l) |  Т3 GENERAL  (nmol/l) |
| Newborns |   11,6 – 35,9 |   105 - 290 |     21 – 49 |   0,84 – 3,63 |
| Childern:      2 days      3 days      1 weeks      2 weeks      3 weeks      1 month      6 months      1 year old      5 years old      10 years old      15 years old |     8,3 – 19,8   1,0 – 10,9   1,2 – 5,8       0,7 – 6,4   0,7 – 6,4   0,7 – 6,4   0,7 – 6,4   0,7 – 6,4 |      83 – 303    110 – 285     93 – 247     88 – 225     94 – 259    112 – 243    103 – 210     92 – 189     89 – 173     71 – 145     64 - 149 |      21 – 38    19 – 37    18 – 35    18 – 35    17 – 33    16 – 33    15 – 29    14 – 23    13 – 23    12 – 22    12 - 23 |    1,95 – 3,63  0,81 – 3,39  0,65 – 1,90  0,59 – 1,84  0,77 – 2,15  1,10 – 3,10  1,43 – 3,17  1,75 – 3,50  1,80 – 3,10  1,70 – 3,10  1,50 – 2,80 |
| Adults:    Younger than 60     Older than 60  |     0,3 – 4,0   0,5 – 7,8 |      50 – 150    65 - 135 |      10 – 25    10 - 18 |      1,0 - 3,0  0,62 – 2,79 |
| Pregnant women:    1 three-month    2 three-month    3 three-month |     0,3 – 4,5   0,5 – 4,6   0,8 – 5,2 |         79 - 227 |     |  |

2 or 3 days before the examination, if there is no special instruction of the endocrinologist, the intake of iodine-containing drugs shall be stopped and 1 month before, the intake of thyroid hormones (to obtain the true basal levels) shall be stopped. If the purpose of the examination is to control the dose of thyroid hormone preparations, a blood sample is taken against the background of taking the prescribed dose of the drug. It should be taken into account that taking levothyroxine causes a transient increase in the amount of total and free thyroxine in the blood (15-20%) for about 9 hours.

**THYROTROPHY HORMONE (TTH or TSH)**

TSH is considered as the main criterion in the laboratory assessment of thyroid gland function. If there is a suspicion of a change in the hormonal activity of the gland, the diagnosis should be started with the determination of TSH. TSH is a glycoprotein that is synthesized in the anterior part of the pituitary gland and stimulates the synthesis of thyroglobulin, the formation and secretion of thyroid hormones. TSH secretion is very sensitive to changes in serum T3 and T4 concentrations. A 15-20% decrease or increase in this concentration causes reciprocal changes in TSH secretion (the principle of feedback).

The presence of dependence on the formation and secretion of TSH from the effect of drugs, the daily rhythm of changes in the TSH level, the state of stress and the presence of somatic diseases in the patient should be taken into account when examining the results of the examination.

INDICATIONS for determination of TSH:

* dysfunction of the thyroid gland, various types of hypothyroidism, hyperthyroidism, retardation of mental and sexual development in children, arrhythmias, myopathy, depression, alopecia, infertility, amenorrhea, hyperprolactinemia, impotence and decreased libido;
* monitoring of the condition of patients against the background of hormone replacement therapy: During replacement therapy, blood should be taken for the examination of TSH 24 hours after taking the medicinal product;
* congenital hypothyroidism screening: TSH level in blood serum is determined on the 5th day of the child's life. If the TSH level is greater than 20 mIU/L, a new blood sample should be taken and tested again. If the concentration of TSH fluctuates between 50 and 100 mIU/l, there is a high probability of the disease. Congenital hypothyroidism is characterized by a concentration of TSH above 100 mIU/L.

**CLINICAL DIAGNOSTIC SIGNIFICANCE OF TTH**

In treated hyperthyroid patients, TSH levels may be low for 4-6 weeks after reaching a euthyroid state.

TSH synthesis may be impaired in critically ill patients with normal concentrations of T4 and T3.

TSH secretion is attenuated during thyroxine treatment and during post-operative replacement therapy. In such cases, a normal or high level of TSH indicates a low dose of the drug, peripheral resistance to thyroid hormones, or the presence of antibodies against thyroid hormones. During hypothyroidism, the optimal TSH level should be lower than the reference values.

**THYROXINE ( ​​T4 )**

Thyroxine is a thyroid hormone, whose biosynthesis occurs in the follicular cells of the thyroid gland under the control of TSH. The main part of organic iodine in the blood is in the form of T4. About 70% of T4 is bound to globulin, 20% to prealbumin, and 10% to albumin. Only 0.02 - 0.05% of T4 circulates in the blood unbound to protein (the free part of T4). The concentration of T4 in serum depends not only on the rate of secretion, but also on the amount of proteins. Free T4 makes up 0.02 - 0.04% of total thyroxine.

**PATHOLOGIES ACCOMPANIED BY A CHANGE OF THE LEVEL OF T4 IN THE BLOOD**

Hunger, protein-poor diet, lead poisoning, strenuous muscular exercise, excessive physical work, stress, weight loss in obese women, surgical operations, hemodialysis can cause a decrease in total and free T4. Hyperemia, obesity causes an increase in T4.

**DISEASES ACCOMPANIED BY CHANGE OF TOTAL T4 LEVEL IN THE BLOOD**

The concentration of total T4 increases:

- HIV infections, acute and subacute hepatitis;

- Hyperthyroidism, conditions accompanied by an increase in TSH (pregnancy, genetic predisposition, acute intermediate porphyria, primary biliary cirrhosis).

- Hyperestrogenia (as a result of an increase in TSH, total T4 increases, while the level of free T4 remains normal);

- Diffuse toxic goiter;

- Obesity;

- Acute mental disorders;

- Acute thyroiditis;

- Thyroid hormone resistance syndrome;

- Thyrotropinoma;

- Toxic adenoma;

- TSH-independent thyrotoxicosis;

- Choriocarcinoma

**CLINICAL DIAGNOSTIC SIGNIFICANCE OF T4**

An increase in total T4 in the background of normal TSH and T3 can rarely occur. It is seen in patients with normal thyroid function but congenitally oversynthesized thyroid hormone-carrying proteins in the liver.

In the initial stage of hypothyroidism, the level of free T3 decreases faster than total T4. The diagnosis is confirmed when TSH increases.

A normal T4 level may not indicate normal thyroid function. T4 may be normal in endemic goiter, suppressive or replacement therapy, hidden forms of hyperthyroidism or hypothyroidism.

During thyrostatic therapy, the presence of T4 at the level of the upper limit of the norm indicates the adequate selection of the maintenance dose.

Elevated free T4 levels do not always indicate thyroid dysfunction. It can also be related to taking certain medications or serious general illnesses.

**TRIODOTHYRONINE (​​T3)**

Triiodothyronine is a thyroid hormone that consists of 58% iodine. A part of serum T3 is formed as a result of enzymatic deiodination of T4 in peripheral tissues, only a small part is directly synthesized in the thyroid gland. Less than 0.5% of circulating T3 in serum is in free form and is biologically active. The remaining T3 is combined with serum proteins (TSH, prealbumin and albumin). The affinity of T3 to serum proteins is 10 times lower than that of T4. In this regard, the free T3 level does not have as much diagnostic value as the free T4 level. At least 80% of circulating T3 is derived from monodeiodination of T4 in peripheral tissues. T3 is 4-5 times more active than T4 in biological systems. Because T3 levels fluctuate rapidly under the influence of stress or other non-thyroid factors, measuring T3 is not considered as the best test for determining thyroid status. Free T3 makes up about 0.2-0.5% of total T3.

**INDICATIONS FOR DETERMINATION OF T3:**

* differential diagnosis of thyroid gland diseases;
* control examination during isolated T3-toxicosis;
* the early stage of hyperfunction of the thyroid gland;
* after treatment with thyroxine during acute hyperthyroidism;
* recurrence of hyperthyroidism;
* to prevent drug overdose.

**CLINICAL DIAGNOSTIC SIGNIFICANCE OF T3**

During iodine deficiency, a compensatory increase in total and free T3 is observed. Thus, the body adapts to iodine deficiency. Sufficient iodine supply leads to normalization of T3. No treatment is required in these individuals. In hypothyroidism, total and free T3 levels may be in the subnormal range for long periods of time because increased conversion of T4 to T3 compensates for decreased T3.

TSH and T3 levels are measured to avoid overdose during treatment of goitre or post-operative thyroxine replacement therapy.

In the treatment of hypothyroidism with thyroxine, T3 increases less than T4. When using large doses of thyroxine, TSH decreases to an undetectable level. Analysis of the T3 level is carried out to prevent overdose of drugs.

At the beginning of thyrostatic therapy, the level of T3 may increase due to compensatory processes.

Serum T3 levels are less specific for hypothyroidism because activation of the conversion of T4 to T3 keeps T3 levels in the normal range until severe hypothyroidism develops. T3 levels decrease in patients in a state of energy starvation. Elevated T3 levels are an early sign of Graves' disease relapse. Elevated or normal T3 levels are seen in cordaroin-induced hyperthyroidism.

**THYROGLOBULIN (TG)**

Thyroglobulin is a glycoprotein containing iodine. TG is the main component of the colloid of thyroid follicles. Thyroid hormones are synthesized on the surface of TG. TG secretion is regulated by TSH.

**DISEASES AND CONDITIONS THAT CAUSE CHANGE IN BLOOD TG LEVELS**

An increase in the amount of thyroglobulin in the blood indicates a violation of the integrity of the hematothyroid barrier, it is observed in diseases accompanied by a violation of the structure of the gland or iodine deficiency. During the stimulation of the thyroid gland and its structural damage, the transfer of TG into the blood increases. The determination of TG within 2-3 weeks after a puncture biopsy is not important, because the level of TG may increase as a result of the passive transfer of colloid to the blood during traumatic damage to the gland. Thyroglobulin levels rise shortly after thyroid surgery. The level of thyroglobulins may increase in diffuse toxic goiter, in subacute thyroiditis, during thyroid gland enlargement under the influence of TSH, and in benign adenoma of the thyroid gland.

The presence of anti- TG antibodies can cause false negative results, so it is advisable to determine anti- TG antibodies in parallel with TG.

In patients with undifferentiated thyroid cancer, the concentration of TG in the blood rarely increases. In differentiated tumors with low functional activity, TG level increases less than in tumors with high functional activity. Determining the level of TG is of great diagnostic importance for the detection of metastases of thyroid cancer and the dynamic monitoring of the condition of patients during the treatment of follicular carcinoma. Thyroid cancer metastases have also been found to have the ability to synthesize TG.

A decrease in the level of thyroglobulin in the blood after surgery or radiation therapy denies the presence of metastases. On the contrary, an increase in the level of TG may be a sign of a generalized process.

After radical treatment of differentiated thyroid cancer, patients receive high doses of thyroid hormones (to weaken TSH secretion), TG level also decreases, its concentration in serum should be determined 2-3 weeks after cancellation of suppressive therapy with thyroid hormones.

In the treatment of children with congenital hypothyroidism, the determination of TG is of great importance for the selection of the dose of hormone replacement therapy. In aplasia of the thyroid gland (when TG is not detected in the blood), the maximum dose is prescribed, while in other cases, an increase in the concentration of TG indicates a reversible course of the disease, and therefore the dose of the hormone is reduced.

TG cannot be determined for the purpose of differential diagnosis of tumors.

**ANTIBODIES TO THYROGLOBULIN (ANTI-TG).**

The thyroid gland, which has specific antigens, can make the body's immune system into a state of autoaggression. One such antigen is thyroglobulin. Damage to the thyroid gland during autoimmune or neoplastic diseases can cause TG to enter the bloodstream, which in turn leads to the activation of the immune response and the synthesis of specific antibodies. The concentration of anti-TG varies widely and depends on the disease. Therefore, the determination of anti-TG concentration can be used to monitor the diagnosis and treatment of thyroid diseases.

**INDICATIONS FOR DETERMINATION OF ANTI-TG:**

- newborns: high anti-TG titer in the mother,

- chronic Hashimoto's thyroiditis,

- differential diagnosis of hypothyroidism,

- diffuse toxic goiter (Graves' disease),

- when postoperative treatment of patients with highly differentiated thyroid cancer is carried out in a complex manner with TG,

- in areas with iodine deficiency,

REFERENCE limit - 0 - 100 mU/ml

**ANTIBODIES AGAINST THYROID PEROXIDASE (ANTI - TPO).**

The anti-TPO test is used to detect autoimmune thyroid diseases. Anti-TPO, which has the property of binding to complement, is directly involved in autoaggression, that is, it is an indicator of the aggression of the immune system against its own body. Thyroid peroxidase ensures the formation of the active form of iodine, which is included in the process of iodination of thyroglobulin, that is, plays a key role in the synthesis of thyroid hormones.

Anti-TPO is the most sensitive test for detecting autoimmune thyroid diseases. Usually, its detection is considered as an initial criterion during the development of hypothyroidism caused by Hashimoto's thyroiditis.

**INDICATIONS FOR THE APPOINTMENT OF ANTI-TPO**

- autoimmune thyroiditis,

- prediction of the risk of hypothyroidism with an isolated increase in TSH level,

- postpartum thyroiditis in women from high risk groups,

- ophthalmopathy: "euthyroid Graves' disease".

- newborns: hyperthyroidism and the presence of high anti-TPO titer or Graves' disease in the mother,

- the risk of developing thyroid dysfunction during therapy with interferon, interleukin-2, lithium preparations, cordarone, etc.

REFERENCE INDICATORS – 0 – 30 mU/ml.

**ANTIBODIES AGAINST MICROSOMAL FRACTION (ANTI-MF).**

Antibodies against the microsomal fraction are detected in all types of autoimmune thyroid diseases, as well as in healthy individuals. Anti-MF is a cytotoxic factor that directly damages thyroid cells. Microsomal antigen is a lipoprotein that forms the membranes of follicles containing thyroglobulin. Autoimmune thyroiditis is a disease characterized by the formation of antibodies against various components of the thyroid gland, the development of lymphoid infiltration and fibrotic tissue. Anti-MF destroys the thyroid gland and reduces its functional activity.

**INDICATIONS FOR THE APPOINTMENT OF ANTI-MF**

- Hashimoto's thyroiditis,

- autoimmune diseases of the thyroid gland,

- postpartum thyroiditis in high-risk women

- high risk of developing thyroiditis in case of hereditary predisposition to this disease, in other forms of autoimmune processes (type I diabetes, Addison's disease, pernicious anemia).

**ANTIBODIES TO THE TSH RECEPTOR (TSH-RP)**

Thyrotropic hormone TSH receptors are membrane structures of thyrocytes. TSH-RP are regulatory proteins integrated into the thyroid cell membrane that affect both TSH synthesis and secretion and cell growth. They combine with pituitary TSH and ensure its biological effect. The reason for the development of diffuse toxic goiter (Graves' disease) is the detection of specific immunoglobulins in the blood of patients - autoantibodies that can bind to thyrocyte receptors and have a stimulating effect on the thyroid gland, such as TSH. Detection of a high titer of autoantibodies against TSH receptors in the blood of patients with Graves' disease is an indicator of disease relapse (85% sensitivity and 80% specificity). If the mother suffers from Graves' disease, the fetoplacental transfer of these antibodies leads to the development of congenital hyperthyroidism in newborns.

A high titer of autoantibodies against TSH receptors can be detected in patients with Hashimoto's disease, subacute autoimmune thyroiditis. During the treatment of these diseases or after thyroidectomy, the level of autoantibodies gradually decreases.