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Thyroid function disorders

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Abstract

Thyroid function disorders are the most common endocrine disorders in humans. They are frequently diagnosed, with prevalence varying between 2 and 6%, and a female to male ratio of up to 10:1. Disorders of thyroid function in the narrower sense are presented by its hyperactivity or underactivity, although there are conditions that lead to an increased concentration of thyroid hormones, without its increased activity. In iodine-sufficient regions, the most common cause of hyperthyroidism, as well as hypothyroidism, is an autoimmune disease of the thyroid. For hyperthyroidism, it is Graves' disease, with typical symptoms and signs of hypermetabolism. The diagnosis of hyperthyroidism is based on suppressed TSH and elevated fT4 (free, and in the differential diagnosis, elevated TSH-receptor-antibodies are crucial for Graves' disease. Management of Graves' disease relies on three equally potent approaches: medical therapy, ablative treatments with ^{131}I-radiotherapy-RAI, and thyroidectomy. Hashimoto's thyroiditis is the most common cause of hypothyroidism in iodine-sufficient regions. Symptoms and signs of hypothyroidism are non-specific and correspond to the symptoms and signs of hypometabolism. The diagnosis is made based on elevated TSH with decreased fT4. Thyroxine-peroxidase-antibodies and thyroglobuline-antibodies are important in differential diagnosis. Sometimes elevated TRAb is found in Hashimoto's thyroiditis. The treatment of hypothyroidism is levothyroxine replacement therapy.

Keywords: hyperthyroidism, thyrotoxicosis, hypothyroidism, Hashimoto's thyroiditis, Graves' disease.

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The thyroid gland is one of the largest glands in the human body that plays an important role in tissue metabolism and development. It synthesizes and secretes thyroid hormones, which are essential for growth, neuronal and overall development, reproduction, and regulation of energy metabolism, as well as for all metabolic processes in cells during life. The thyroid gland does not function as an independent organ. Its activity is predominantly under the control of the pituitary gland, that is, thyroid-stimulating hormone (TSH), so the regulation of the thyroid function in healthy people is largely determined by the factors that regulate the synthesis and secretion of TSH. The main influence on TSH synthesis and secretion is exerted by the thyroid hormones themselves, thyroxine (T4) and triiodothyronine (T3) through negative feedback, and thyrotropin-releasing hormone (TRH) through its positive action on thyrotrophs. Hypothalamic TRH regulates the synthesis, secretion, and biological activity of pituitary TSH, which further stimulates all steps in the thyroid hormone biosynthesis and secretion. On the other hand, thyroid hormones (T3 and T4) control the secretion of both TRH and TSH through a negative feedback loop, thus maintaining the physiological values of hypothalamic-pituitary-thyroid (HPT) axis hormones. The consequence of the dynamic interaction of these two dominant influences on TSH secretion is an extremely stable morning circulating concentration of TSH and thyroid hormones, so stable that it is believed that the value of TSH outside the normal range, in most patients, indicates the presence of a disorder in the function of the thyroid gland (1, 2).

Thyroid hormones are essential for cellular energy homeostasis and regulation. They regulate a wide range of genes that are involved in multiple physiological processes, regulate basal metabolic rate, and promote the adrenergic nervous system to generate heat in response to cold exposure. They also play an important role in metabolic processes, by stimulating gluconeogenesis and both lipolysis and lipogenesis, (3, 4), affecting cholesterol synthesis and LDL-receptor expression (5, 6). Abnormal thyroid hormone levels lead to hypothyroid and hyperthyroid states. Hyperthyroidism and hypothyroidism most often occur as a result of pathological processes in the thyroid gland itself, although they can also occur because of excessive or insufficient stimulation of the otherwise healthy thyroid- by the hypothalamus/pituitary, when we talk about secondary (central) hypothyroidism or hyperthyroidism.

Thyroid function disorders are the most common endocrine disorders in humans. They are frequently diagnosed, with prevalence varying between 2 and 6% in large population-based studies (7–10), depending on the region, population, and iodine status. They occur more often in women with a female-to-male ratio from 4 to 1 up to 10 to 1 (11, 12) In both sexes the prevalence increases with age.

Thyrotoxicosis and hyperthyroidism

Thyrotoxicosis represents the appearance of clinical signs and symptoms of hypermetabolism caused by high concentrations of thyroid hormones in the bloodstream and their effect on the periphery, regardless of the cause of their increased concentration.

Hyperthyroidism is a narrower term that indicates the source of increased hormone concentration. It is a hypermetabolic syndrome caused by hypersecretion of thyroid hormones from the thyroid gland. There are different causes of thyrotoxicosis that must be distinguished, because the therapeutic approach depends on its etiology. The causes of thyrotoxicosis can be divided into those involving the increased production of hormones by the thyroid gland and those involving the increased availability of thyroid hormones in the circulation, most often caused by destructive, inflammatory processes in the thyroid gland that lead to the release of preformed, stored hormones from the injured thyroid (Table I).

Table I Causes of thyrotoxicosis
Tabela I Uzroci tirotoksikoze

Thyrotoxicosis with hyperthyroidism (increased thyroid hormone synthesis)	Thyrotoxicosis without hyperthyroidism (increased availability of preformed thyroid hormone)
• Graves disease • Toxic multinodular goiter • Solitary toxic adenoma • TSH-secreting pituitary adenoma • Choriocarcinoma • Hyperemesis gravidarum • Iodine, iodine-containing drugs • Struma ovarii • Thyroid carcinoma	• Subacute thyroiditis • Silent (painless) and postpartum thyroiditis • Drug-induced thyroiditis • Acute infectious thyroiditis • Radiation thyroiditis • Exogenous thyroid hormone

Hyperthyroidism

The most common cause of thyrotoxicosis is hyperthyroidism, and in iodine-sufficient areas it is Graves' disease (GD), which accounts for about 80% of cases (13). The second most common cause of thyrotoxicosis is nodular/multinodular thyroid disease, and the third is thyroiditis. The frequency of these diseases varies greatly depending on iodine intake (in iodine-deficient regions, nodular disease of the thyroid is the cause of thyrotoxicosis in up to 50% of cases) (14), the age of the population (the

incidence of toxic nodular goiter increases with age) (15), and with the region studied (frequency of painless thyroiditis was 0.5% in Denmark vs. 22% in Wisconsin) (16).

Graves' disease

Graves' disease is the most common cause of hyperthyroidism in iodine-sufficient areas and accounts for 60-80% of all hyperthyroidisms. It has an annual incidence of 20 to 50 cases per 100,000 persons (17) and a lifetime risk of 3% in women and 0.5% in men (18).

GD occurs at any age, with the highest risk of onset in the 30 to 50 years of age. It is much more common in women than in men, with the female-to-male ratio between 4:1 and 10:1 (9).

GD occurs as a result of the interaction of genetic and environmental factors. Genetic predisposition plays a very important role in the occurrence of the disease and carries about 79% of the risk, while the share of external factors in the risk of GD is about 21% (smoking, excess iodine, lack of selenium, vitamin D) (19).

Graves' disease is a systemic autoimmune thyroid disease caused by the production of IgG autoantibodies directed against the thyrotropin receptor (TSH-R). These TSH receptor antibodies (TRAb) bind to and activate the receptor, mimicking the effects of the TSH on thyroid cells and causing the autonomous production of thyroid hormones. This activation of the TSH receptor leads to stimulation of the growth of follicular cells, which leads to diffuse enlargement of the thyroid gland and the appearance of goiter, as well as to increased production of thyroid hormones with a change in the ratio of produced thyroxine (T4) and triiodothyronine (T3) in favour of T3 (20).

Clinical presentation

The clinical presentation of hyperthyroidism corresponds to the clinical presentation of hypermetabolism. Since thyroid hormones have an effect on all body cells, signs and symptoms of the disease will occur in all organs and systems.

The symptoms may develop gradually or suddenly and may be mild, sometimes severe. They include weight loss despite increased appetite, increased heart rate, palpitations, frequent bowel movement, diarrhoea, nervousness, anxiety and irritability, reduced concentration, hyperactivity, mood swings, insomnia, fatigue, heat intolerance, excessive sweating, muscle weakness, menstrual irregularity, decreased libido, and infertility (Table II).

Physical signs also may vary and include: tachycardia, warm, soft, moist skin, red palms, onycholysis (Plummers's nails), hair loss or thinning, enlarged thyroid with thrill and bruit, resting hand tremor, hyperreflexia, proximal muscle weakness, and eye problems, such as redness, dryness or vision problems (18,21).

Table II Symptoms and signs of hyperthyroidism
Tabela II Simptomi i znaci hipertireoze

Symptoms of hyperthyroidism	Signs of hyperthyroidism
• increased appetite • weight loss • excessive sweating • heat intolerance • increased heart rate, palpitations • nervousness, anxiety, and irritability • hyperactivity, mood swings • reduced concentration, insomnia • hair loss or thinning • fatigue • frequent bowel movement, diarrhea • muscle weakness • oligomenorrhoea, transient infertility • decreased libido	• warm, soft, moist skin • red palms, onycholysis (Plummers' nails) • tachycardia • systolic hypertension • enlarged thyroid with thrill and bruit • resting hand tremor • hyperreflexia • proximal muscle weakness • eye problems

GD can sometimes be associated with manifestations of extrathyroidal disease that are not related to the circulating level of thyroid hormones, such as Graves' orbitopathy and thyroid dermopathy (localized or pretibial myxoedema). They are caused by the inflammatory process, local tissue infiltration by inflammatory cells and the accumulation of glycosaminoglycans in the tissues (21).

In GD, minor ocular (eye) signs, may be present, such as eyelid retraction ("stare"), extraocular muscle weakness, and lid-lag. These signs are signs of hyperthyroidism, but not of orbitopathy, and should not be confused with it. Graves orbitopathy (GO) is the major extrathyroidal manifestation of GD, but it is not exclusively related to GD because it can also occur in patients with chronic autoimmune thyroiditis although less frequently. Clinically apparent exophthalmos occurs in 30-50% of patients with GD, but if orbital imaging is used, exophthalmos can be detected in over 80% of patients with GD. The clinical course of GO is independent of thyroid function and can appear before, during or after remission of GD, in association with chronic autoimmune thyroiditis and even independently, with normal thyroid function and no thyroid disease. Its manifestations include periorbital edema and inflammation, proptosis, photophobia, extraocular muscle infiltration, and eyelid lag, and in severe cases exposure keratitis and sight loss (22, 23).

One to two months after establishing a euthyroid state, the symptoms, and signs of hypermetabolism disappear in the majority of patients. Symptoms are typically less severe in the elderly and during pregnancy.

The most severe form and life-threatening complication of hyperthyroidism is thyroid storm. This serious complication occurs rarely, in 1-2% of patients with hyperthyroidism, most often as a result of the discontinuation of therapy for hyperthyroidism or the appearance of an acute infectious disease, or acute cardiac event, and is a medical emergency. It is manifested by hyperpyrexia (due to severe thermogenesis), atrial tachyarrhythmias (due to hyperadrenergic response), acute heart failure, mental status changes, and liver dysfunction. The mortality rate is high, 8-25% despite modern and intensive treatment and supportive measures (24, 25).

Diagnosis

The initial evaluation of suspected thyroid dysfunction is the measurement of serum baseline TSH as the acknowledged screening parameter. Free thyroid hormones differentiate overt and subclinical hyperthyroidism/thyrotoxicosis (26). The specific marker of GD is TRAb, which is of key importance for the differential diagnosis of thyrotoxicosis and hyperthyroidism and enables the rapid diagnosis of GD. Ultrasonography with color-flow Doppler supports the diagnosis of GD as a non-invasive, rapid, and accurate imaging procedure. It shows a diffusely enlarged hypoechoic thyroid gland with a markedly increased CD signal ("thyroid inferno"). Technetium-labeled thyroid scintigraphy shows an increased thyroid uptake of radioactive iodine (24) and can be used when the cause of hyperthyroidism is uncertain. It can very accurately differentiate hyperthyroidism caused by GD or multinodular/nodular toxic goiter, as well as thyroiditis.

Treatment

Management of GD relies on three equally potent approaches: medical therapy - antithyroid drugs, ^{131}I-radiotherapy-RAI or thyroidectomy. The last two represent ablative treatment because they remove or decrease thyroid tissue. Considering that the therapy is not causal but is aimed at the reduction of the synthesis and secretion of thyroid hormones, a large number of patients face either a relapse of the disease or the development of definite hypothyroidism. (27).

Medical treatment

Antithyroid drugs (ATDs) affect all parts of thyroid synthesis and secretion. They inhibit the transport of iodine into the cell, the organification of iodine, and its incorporation into iodotyrosines. There are three compounds available: methimazole (MMI), carbimazole (an inactive drug, 2-fold weaker than MMI that is rapidly metabolized in the blood to MMI), and propylthiouracil (PTU). PTU is 10-fold weaker than MMI, however, it additionally inhibits the peripheral conversion of T4 to T3. MMI

has the longest half-life and acceptable and low side-effect profile. It is, therefore, regarded as the preferred ATD with the highest efficacy; the use of PTU is restricted to patients who cannot tolerate other thioamides and to women in the first trimester of pregnancy due to its less teratogenic effects (28). The most common initial type of treatment for hyperthyroidism in Europe, Asia and Latin America is medical treatment, while the most common initial treatment in America is RAI (29). The initial dose of ATDs usually ranges from 15 to 30 mg of MMI and depends on the initial severity of the disease as well as the degree of patient response to treatment. Monitoring of thyroid function tests is initially recommended after 4 weeks and then 2- to 3-monthly thereafter. The dose of MMI is gradually reduced to the optimal maintenance dose and may eventually be reduced to a daily maintenance dose of 5 mg. Usually, ATDs are administered for 12 to 18 months (24). For the discontinuation of thionamides therapy, it is necessary to achieve both clinical and biochemical as well as serological remission, i.e., to maintain the achieved euthyroidism and for TRAb levels to become negative.

RAI treatment

In Europe, RAI treatment is used in case of failure of medical initial treatment or intolerance of ATDs, while in the United States RAI is most often used as an initial treatment. After RAI treatment, approximately 80% of patients eventually become hypothyroid, 10% remain euthyroid, and 10% will need a second (or even a third) ablative dose (30). Special caution is needed in patients with GO because RAI treatment may worsen the course of GO. In most cases, in active GO, RAI therapy is not recommended, or, if necessary, protective doses of corticosteroids (prednisolone 30-50 mg/day) are advised for these patients, starting on the first day of RAI treatment with a gradual dose reduction over the next 6- 8 weeks (31).

Surgery

Surgery is recommended for patients who refuse or cannot tolerate treatment with thioamides or RAI, those with large, compressive goiters or suspicious nodules, and patients with active, severe GO. The most common type of surgery for achieving remission is total, but it carries operative risks related to general anaesthesia, paralysis of the recurrent laryngeal nerve, and transient or permanent hypoparathyroidism.

Hypothyroidism

Hypothyroidism is a chronic disease associated with a deficiency in the thyroid hormones, thyroxine (T4) and triiodothyronine (T3), in target tissues, irrespective of its cause (32). Primary hypothyroidism occurs as a result of pathological processes in the thyroid gland itself, which lead to disturbances in the synthesis and secretion of thyroid hormones. Because of the reduced thyroid hormones secretion, there is an increase in the concentration of TSH in the circulation. Hypothyroidism can be caused by insufficient TSH stimulation of the thyroid gland, which can occur as a result of pathological processes in the pituitary gland or hypothalamus (secondary and tertiary hypothyroidism).

These two forms of hypothyroidism are called central hypothyroidism. The precise prevalence of central hypothyroidism is unknown but has been estimated to range from 1:16,000 to about 1:100,000 in the general adult or neonatal populations (33).

Primary hypothyroidism is a very prevalent disease worldwide. It can be endemic in iodine-deficient regions, but it is also a common disease in iodine-replete areas. In iodine-replete areas, the prevalence of spontaneous hypothyroidism is between 1 and 2%, and it is 10 times more common in women than in men and more common in older women (34). In their meta-analysis from 2014, Garmendia Madariaga et al. showed that the prevalence of overt and subclinical hypothyroidism in Europe was 0.37% and 3.8%, respectively, including both diagnosed and undiagnosed cases, and the estimated incidence of hypothyroidism was 226 cases per 100,000 individuals per year (8). The incidence of hypothyroidism also increases with the introduction of iodine supplementation, because too high iodine levels as well as too low are unsafe and can lead to compromised hormone synthesis and autoimmune thyroiditis, especially for susceptible populations (35). The most common cause of primary hypothyroidism in iodine-sufficient regions is a chronic autoimmune disease, Hashimoto's thyroiditis.

Table III Causes of primary hypothyroidism
Tabela III Uzroci primarne hipotireoze

Loss of functional thyroid tissue	Functional defects in thyroid hormone biosynthesis and release
• Chronic autoimmune thyroiditis • Reversible hypothyroidism (subacute and postpartum thyroiditis) • Surgery and irradiation • Infiltrative and infectious diseases • Thyroid disgenesis	• Congenital defects in hormone biosynthesis • Iodine deficiency and iodine excess • Drugs (ATDs, lithium, tyrosine kinase inhibitors, goitrogenic chemicals

ATDs – antithyroid drugs;
ATDs – antitiroidni lekovi;

Hashimoto's thyroiditis

The term chronic autoimmune thyroiditis most often refers to Hashimoto's thyroiditis, although there is also an atrophic type of autoimmune thyroiditis called Ord's

thyroiditis. Although with the same etiology and pathogenesis, these two types of autoimmune thyroiditis are called differently. While Hashimoto's thyroiditis first presents with a goiter, Ord's thyroiditis is characterized by thyroid atrophy from the beginning. Finally, the end stage of both types of autoimmune thyroiditis is atrophy of the thyroid gland. Since **i**n primary autoimmune hypothyroidism thyroid volume follows a normal distribution, some argue that they represent two extremes of the same disease and should be classified together as a combined "Ord-Hashimoto's disease" (36).

Pathogenesis

Genetic and environmental factors play a role in the development of chronic autoimmune thyroiditis. Of the environmental factors, micronutrients are of importance for the development of autoimmune thyroiditis (mainly iodine and selenium), as well as drugs, infection, radiation therapy of the neck, and endocrine disruptors also play an important role, contributing to the expansion of autoreactive T lymphocytes.

Autoimmune thyroid disease (ATD) is characterized by lymphoid infiltration of the thyroid gland, including T and B cells. Both, cellular and humoral immunity have a role in the pathogenesis of thyroid autoimmunity. Increased activation of follicular helper T cells as well as defects in T regulatory lymphocytes might be the initial point of the disease and its amplification. Lymphocytes that infiltrate the thyroid gland can be directly cytotoxic to thyroid follicular cells or may affect cell viability and function indirectly through cytokine production. Cytokines produced by lymphocytes infiltrating the thyroid tissue play a major role in thyrocyte damage. These cytokines also induce thyrocytes themselves to produce pro-inflammatory cytokines, which lead to amplification of inflammation and induction of an autoimmune inflammatory response. (37). Humoral immunity plays a role in the production of autoantibodies. Antibodies against thyroxine-peroxidase (TPO Ab) and thyroglobulin antibodies (TgAb) are present in almost all patients with autoimmune thyroiditis. In patients with chronic autoimmune thyroiditis, blocking as well as stimulating TRAb can also be found, and the balance between them may explain the fluctuation of the thyroid hormone levels in some patients with ATD, as well as the restoration of euthyroidism in some patients. While blocking TRAb causes thyroid atrophy and hypothyroidism, TPOAb and TgAb do not necessarily cause hypothyroidism. The biological effect of TRAb can be evaluated based on the clinical presentation: the occurrence of GO in autoimmune thyroiditis speaks in favor of stimulating TRAb, while the reduction of the gland volume and the occurrence of atrophic thyroiditis before the development of fibrosis and the reduction of the goiter speak for the blocking effects (38).

Clinical presentation

Since thyroid hormones affect every cell in the body, hypothyroidism affects all organs and , inducing signs and symptoms of generalized hypometabolism. Clinical manifestations of hypothyroidism depend on the degree of thyroid hormone deficiency, and occur as a result of two pathological processes: a decrease in the intensity of

metabolic processes, which gives symptoms such as fatigue, cold intolerance, bradycardia, constipation, or the accumulation of glycosaminoglycans in the interstitial tissue, which leads to the appearance of weight gain, elastic edema, and hoarseness of voice.

The onset of hypothyroidism in most cases is gradual. Therefore, symptoms and signs can be vague and non-specific (Table IV). Since they are nonspecific, they can overlap with symptoms of non-thyroid origin. They include fatigue or tiredness, dry skin, weight gain, and constipation due to reduced gastrointestinal motility. Decreased motility is also a probable cause of gallbladder hypotonia and bile duct stone formation (39). Some patients develop a goiter, while others have a normal-sized or small firm thyroid.

Table IV Symptoms and signs of hypothyroidism
Tabela IV Simptomi i znaci hipertireoze

Symptoms of hypothyroidism	Signs of hypothyroidism
• decreased appetite	• swelling of the face, hands, feet
• weight gain	• hoarseness, slow speech
• generalized swelling	• cold dry, pale, thickened skin
• cold intolerance	• goitre
• dry, cold, pale, cracked, yellowish skin	• bradycardia, diastolic hypertension
• brittle, coarse hair and nails	• pericardial effusion
• bradycardia	• pleural effusion, hypoxia
• dyspnoea, sleep apnoea	• hyporeflexia, deafness, cognitive dysfunction
• fatigue and tiredness	• galactorrhea
• drowsiness, impaired memory, depression	**Biochemical characteristics**
• slow bowel movement, constipation	• anemia, tendency to bleed
• muscle spasms, myalgia, joint pains	• impaired glomerular filtration/renal failure
• neuropathies, carpal tunnel syndrome	• hyperlipidemia
• hoarseness	• mild hepatocellular dysfunction
• menometrorrhagia, transient infertility	• non-alcoholic fatty liver disease
• decreased libido	• hyponatremia

The most extreme form of hypothyroidism that can cause death unless diagnosed and treated promptly is myxedema crisis/myxedema coma. It is a rare, life-threatening clinical condition with a mortality rate up to 50–60% if diagnosed late, despite intensive treatment and supportive care (40). It occurs most often in older age, more often in women

than in men, and it is most often precipitated by infection, cerebrovascular disease, heart failure, trauma, or medications.

Diagnosis

Since the symptoms are not specific to hypothyroidism and have low sensitivity and positive predictive value, diagnosis of primary hypothyroidism is made by finding elevated TSH and decreased fT4 levels (41). Since the most common cause of primary hypothyroidism is chronic autoimmune thyroiditis, elevated TPOAb and TgAb can be found in most patients, although it should be borne in mind that about 10% of the general population may have elevated thyroid-specific antibodies without consequences for thyroid function (42). On the other hand, autoimmune thyroiditis may exist in the absence of detection of thyroid-specific antibodies in about 10% of patients with Hashimoto's thyroiditis. The vast majority of patients with positive thyroid-specific Ab are euthyroid. Approximately 10% of those with positive TPOAb and/or TgAb have hypothyroidism (38).

Treatment

Levothyroxine (LT4) therapy is the mainstay of treatment for hypothyroidism. It is a once-daily orally active hormone replacement therapy.#Typical full replacement doses in adults are between 1.4 and 1.7 mcg/kg body weight per day (43), but lower starting doses should be used in older individuals, those with untreated cardiovascular disease, or those with mild hypothyroidism. It has a favourable side effect profile, ease of administration, good intestinal absorption, long serum half-life, and low cost. Levothyroxine therapy leads to improvement of the general condition and disappearance of hypothyroidism symptoms in the majority of patients, although some symptoms, given their non-specificity, may persist. At the start of treatment, the dose of LT4 required to normalize TSH levels varies from patient to patient and is largely dependent on the amount of residual endogenous thyroid function and the patient’s weight, mainly lean body mass (43). The goal of therapy is to normalize TSH levels. After the initiation of therapy, thyroid hormone status checking must be frequent, initially after 6 weeks, and after achieving optimal TSH, at 6-12 months. In case of dose correction, thyroid hormone checking should also be after 6-8 weeks. LT4 should be taken regularly, on an empty stomach, separately from food, drinks and other medications, preferably in the morning, 30-60 minutes before breakfast. Since the therapy is lifelong, the importance of taking the therapy regularly must be explained to the patients in order to avoid the risk of overdosing and underdosing. Special attention is needed in pregnant women when titrating the dose of levothyroxine, since thyroid hormones are necessary for proper growth and development of the fetus. Maternal thyroid hormones are essential for fetal growth and development, especially in the early gestational period up to 16-10 gestational weeks, a critical period for fetal brain development. Due to the increase in thyroid hormone production during pregnancy, there is a need to increase the dose of LT4 in pregnant women at the beginning of pregnancy. To maintain euthyroidism during

pregnancy, the dose should be increased by 25-50%. In the period before conception and during the first trimester, TSH should be lower than 2.5 mIU/L. Serum TSH levels should be closely monitored, approximately every 4 weeks during the first half of gestation (44).

Although there has been great progress in the field of understanding the metabolism and action of thyroid hormones, we are still unable to apply some of this knowledge in clinical practice. Levothyroxine therapy has been shown to be an effective way of thyroid hormone replacement in most patients. The majority of them can successfully replenish their thyroid hormones with LT4 treatment. A small percentage of patients still experience symptoms like fatigue, weight gain, memory and thinking issues, and mood disorders even after their fT4 and TSH levels have stabilized on replacement therapy. Since studies have shown that LT4 monotherapy is associated with lower T3 levels (45), it is advised to consider combined T4+T3 therapy in patients with recurrent symptoms (46).

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Poremećaji funkcije štitaste žlezde

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Kratak sadržaj

Poremećaji funkcije štitaste žlezde su najčešći endokrini poremećaji kod ljudi. Dijagnoza se postavlja često, sa prevalencom 2-6% i značajno su češći kod žena nego kod muškaraca, sa odnosom žene: muškarci i do 10:1. Poremećaji funkcije štitaste žlezde u užem smislu predstavljaju njenu hiperaktivnost ili smanjenu aktivnost, mada postoje stanja koja dovode do povećanja koncentracije tiroidnih hormona u krvi, bez povećane aktivnosti štitaste žlezde. Najčešći uzrok kako hipertireoze tako i hipotireoze u jod suficitnim regionima je autoimunska tiroidna bolest. Najčešći uzrok hipertireoze je Grejvsova bolest sa tipičnim simptomima i znacima hipermetabolizma. Dijagnoza hipertireoze se postavlja na osnovu suprimovanog TSH i povišenih vrednosti fT4, a za diferencijalnu dijagnozu, povišena TSH-receptorska-antitela (TRAt) su ključna za dijagnozu Grejvsove bolesti. Lečenje Grejvsove bolesti se zasniva na tri jednako efektivna pristupa: medikamentno lečenje, ablativna terapija radioaktivnim jodom ili tiroidektomija. Hašimoto tiroiditis je najčešći uzrok hipotireoze u jod suficitnim regionima. Simptomi i znaci hipotireoze su nespecifični i odgovaraju simptomima i znacima hipometabolizma. Dijagnoza se postavlja na osnovu povišenih vrednosti TSH uz snižen fT4, a u diferencijalnoj dijagnozi od značaja su antitela na tiroksin peroksidazu (TPOAt) i tiroglobulinska antitela (TgAt), mada se ponekad i u Hašimoto tiroiditisu mogu naći povišena TRAb. Lečenje se sprovodi supstitucionom terapijom levotiroksinom.

Ključne reči: hipertireoza, tirotoksikoza, hipotireoza, Hašimoto tiroiditis, Grejvsova bolest