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CONDITION OF THE THYROID GLAND IN FORMATION DYSHORMONAL DISEASES OF THE MAMMARY GLAND

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SUMMARY

The thyroid gland is one of the organs of the neuroendocrine system, which has a significant influence on a variety of physiological and cellular functions, including growth, development and metabolism in general. Thyroid diseases are among the most common endocrine disorders in clinical practice, which determines their general pathological significance. It is known that all forms of thyroid diseases occur in women 4–5 times more often than in men. Recent years have been marked by an increase in the prevalence of both thyroid pathology and associated pathology of the reproductive system.

KEYWORDS. ***t thyroid hormones, functional state of the thyroid gland, mastopathy, dyshormonal diseases of the mammary gland, fibrocystic disease.***

RELEVANCE

The mammary glands, as an integral part of the reproductive system of the female body, are a kind of target for the active influence of ovarian sex steroid hormones, tropic hormones of the pituitary gland and, indirectly, hormones of other endocrine glands. Among various hormonal-dependent diseases of the reproductive system, damage to the mammary gland is the most common (according to various sources, up to 60–95%) and, as a rule, is the first to manifest such disorders. This is due to the anatomical and physiological features of the structure of mammary gland tissue and the predominance of the glandular component in the structure. Pathological changes in the mammary glands should be considered as a marker of emerging general hormonal disorders in the regulatory system of the reproductive organs, which, of course, require corrective therapy [5–7, 11–13, 18, 21].

Mastopathy (as defined by WHO, 1984) is a fibrocystic disease characterized by a violation of the relationship between the epithelial and connective tissue components, a wide range of proliferative and regressive changes in the tissues of the mammary gland.

The etiology and pathogenesis of mastopathy is currently not fully understood, although the fact that this pathology is hormonally determined today is considered irrefutable. This is reflected in the fact that in recent years the term " dishormonal diseases of the mammary glands" has been used more often in the literature, since it better reflects the essence of the pathological processes occurring in the organ and explains the increasing interest in this problem on the part of gynecologists and endocrinologists [6, 15, 16, 21].

The relevance of the problem of dishormonal diseases of the mammary gland is due to both their high frequency in the population and the fact that some proliferative forms with epithelial hyperplasia are considered as increased risk factors for the development of breast cancer . The risk of developing breast cancer against the background of mastopathy increases 4–9 times, and according to some literature sources - even 37 times, and the frequency of malignancy increases with cystic changes, calcification , as well as with proliferative processes in the epithelium lining the ducts and cyst walls [11–13, 21, 32].

Several levels of regulation of the functional and morphological state of the mammary glands can be distinguished: a) hormonal, represented by influence pathways through the hypothalamic-pituitary system, adrenal glands and gonads; b) metabolic, associated with disruption of all types of metabolism; c) neuroregulatory , influencing through changes in the state of the central and autonomic nervous system ; d) immunological, caused by disturbances of immune homeostasis, affecting the systems of nonspecific and specific immune response. However, a decisive role in the development of mastopathy, according to a number of sources, is assigned to disorders of the reproductive system, which are manifested by progesterone deficiency conditions against the background of relative or absolute hyperestrogenism [6–8, 18, 21, 24].

It is interesting to note that no direct relationship was found between the content of sex steroids in the blood serum and the condition of the endometrium and mammary glands in women of childbearing age. It remains unclear why dysplastic processes do not affect the entire mammary gland, but only certain parts of it. Since mastopathy is formed against the background of a preserved menstrual cycle and reproductive ability, the determining significance in the development of dishormonal processes in the mammary glands, as in other target organs of sex hormones, is not the absolute value of the level of hormones in the plasma, even in free form, but the local state of the receptors for sex steroids in gland tissue. It is believed that it is the activity of the receptor apparatus that determines the occurrence of the pathological process. Hormonal imbalance causes morphofunctional restructuring of

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the mammary glands, but in some women these changes may not go beyond physiological options, while in others, under conditions of activation of the receptor apparatus of the glands, they can turn into a pathological process [9, 16, 24].

There is no doubt that the normal activity of the thyroid gland is a necessary condition for the harmonious functioning of the body. In this regard, the question naturally arises about the influence of the functional state of the thyroid gland on the condition of the mammary glands. A sufficiently large amount of clinical data has been accumulated, confirmed by the results of laboratory studies, indicating a combination of impaired thyroid status with pathology of the mammary glands.

A number of sources indicate the direct influence of thyroid hormones on the process of proliferation of epithelial cells of the lobular-alveolar structures of the mammary gland through regulation of the level of epidermal growth factor receptors [29, 36].

Most authors agree in determining the indirect influence of altered thyroid status on various levels of regulation of the functional and morphological state of the mammary glands indicated above. The functional interaction of the hypothalamus-pituitary-thyroid and hypothalamus-pituitary-gonad systems comes to the fore in the implementation of this influence. It is believed that the highest links in the multi-stage system of endocrine regulation are the suprahypothalamic structures (acting through neurosteroids , neurotransmitters and neuropeptides) and the hypothalamus (influencing the underlying structures through the production of releasing hormones) [9, 18, 20–23].

The function of the reproductive and thyroid systems is regulated by tropic hormones of the anterior pituitary gland: luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, thyroid-stimulating hormone (TSH), which, in turn, are influenced by the hypothalamic-cortical synchronizing system [1, 2 , 15–17, 23, 26]. Many scientific studies have proven that stressful situations, immune disorders, infectious diseases, as well as structural and functional disorders in the hypothalamic-pituitary system can lead to disruption of the biosynthesis of both thyroid and sex hormones, but the mechanisms of these relationships have not yet been clearly defined and represent an object of interest for study.

Analyzing the mechanisms of interaction between the thyroid and reproductive systems, as well as the ways of their joint influence on the condition of the mammary gland, several main points can be highlighted.

Dysfunction of the hypothalamic-pituitary system can lead to changes in the level of gonadotropic hormones and prolactin. This is due to the similarity in the structure of gonadotropic hormones (LH, FSH) and TSH, which are complex glycoproteins consisting of two subunits. An interesting fact is that the structure of the α - subunits of LH, FSH and TSH is the same, and τηε β - subunit is specific for each hormone and determines its luteinizing , follicle-stimulating or thyroid-stimulating activity only after combining with the α - subunit. The discovered similarity allowed us to draw a conclusion about the emergence of these hormones in the process of evolution from one common predecessor and, accordingly, about the possibility of influence of changes in the content of one on the other.

It is known that τηε ⟨ - subunit, identical in gonadotropic and thyroid-stimulating hormones, protects τηε ⟨ - subunit from the action of proteolytic enzymes, and also facilitates its transportation from the pituitary gland to peripheral target tissues, that is, to a certain extent determines the biological activity of hormones. The significance of this fact is extremely important, since it is known that dysfunction of one or another part of the endocrine system is determined not only by hyper- or hypoproduction of hormones , but also by a decrease in their biological activity against the background of normal levels in the blood serum [16, 23].

In recent years, research *in vitro* and *in vivo* it has been proven that hypothalamic thyrotropin-releasing hormone (THH) is a potential stimulator of the pituitary gland's release of not only TSH, but also prolactin. Although the mechanisms of the releasing effect of TL on thyrotrophs and lactotrophs are different (under the influence of TL, the synthesis of TSH is stimulated by thyrotrophs and its release, and the release of prolactin by lactotrophs , which has already been synthesized previously under the influence of other mediators), the concentrations of thyroxine and triiodothyronine circulating in the blood serum determine the level of prolactin by the mechanism feedback by influencing the production of TL.

Increase in triiodothyronine content (T_3) and thyroxine (T_4) above normal has an inhibitory effect on prolactin levels. Reduced levels of T_3 and T_4 in plasma (for example, in primary hypothyroidism) increase the TL-induced release of prolactin and, accordingly, cause the development of hyperprolactinemic conditions. It is possible that thyrotropin-releasing hormone exerts its stimulating effect on the secretion of prolactin through an increase in the expression of prolactoliberin-releasing genes and receptors for it directly in the adenohypophysis . The condition of hyperprolactinemia in primary hypothyroidism is called Van Wyck– Hoeness –Ross syndrome. Adequate replacement therapy for hypothyroidism with thyroid hormones in this situation leads to normalization of prolactin secretion [2, 10, 16, 30].

Prolactin plays a significant role in the hormonal regulation of morphofunctional changes in the mammary gland. In synergy with other hormones, it controls not only the formation, but also the functional activity of the mammary glands, stimulating lactation. In a number of studies *in vitro* It has been shown that prolactin promotes the active growth of mammary epithelial cells, especially acting in conjunction with progesterone [3, 16, 21, 29].

The lactogenic effect of prolactin increases sharply after childbirth, i.e. against the background of a physiological decrease in the level of estrogen and progesterone. A pathological increase in prolactin levels, leading to increased formation of connective tissue and dilatation of the milk ducts,

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can cause tension, pain, and an increase in the volume of the mammary glands [21].

Research in recent years has established that the cause of the development of dishormonal processes in the mammary gland can be not only an absolute increase in the level of prolactin, but also a disturbance in the rhythm of its daily secretion. The development of the latter is largely due to the high sensitivity of the prolactin secretion system to various kinds of influences. Thus, most pharmaceuticals that have a central effect affect dopamine metabolism and stimulate the secretion of prolactin [16]. This mechanism allows us to explain the fact that the course of mastopathy worsens while taking antidepressants, antipsychotics, etc. We must not forget that hypothyroidism, including subclinical hypothyroidism, often occurs under various "masks", one of which is depressive states. At the same time, inadequate treatment of undiagnosed thyroid pathology with antidepressants and other centrally acting drugs leads to the progression of mastopathy.

In addition to influencing the secretion of prolactin, thyroid hormones can affect the condition of the mammary glands, changing the level of sex hormones.

Normally, cyclic changes in the levels of sex steroid hormones during the menstrual cycle significantly affect the morphofunctional state of the mammary glands. Ovarian hormones (estrogens, progesterone, androgens and inhibin) have a mainly stimulating effect on the proliferation of mammary gland cells [4, 9, 16, 29].

In the follicular phase of the cycle, under the influence of estrogens, cell proliferation occurs in the terminal sections of the ducts. In the luteal phase, due to the influence of progesterone, lobular -alveolar development and cellular differentiation are ensured. The number of estrogen receptors in the epithelium of the mammary glands decreases in the luteal phase, while the density of progesterone receptors remains high throughout the entire cycle. While estrogens increase the size of the mammary ducts by hypertrophy of the lining cells, progesterone causes hyperplasia of these cells by increasing the chemical activity of prelactation compounds in the terminal ducts.

Thus, the first peak of proliferation of the mammary gland epithelium occurs during the follicular phase under the influence of FSH, LH and increased estrogen levels, and the second peak occurs in the middle of the luteal phase at maximum progesterone concentrations. This fact contributes to the fact that in the late luteal phase of the cycle there is a maximum increase in the volume of the mammary glands. However, it should be noted that the peak of mitosis in the luteal phase is replaced by apoptosis.

The ability of thyroid hormones to change the level of sex steroids is due to their effect on the protein-synthesizing function of the liver and stimulation of the production of testosterone- estradiol-binding globulin (TEBL) in the liver, which in the literature is also called sexsteroid-binding globulin, or sex steroid-binding globulin (SHBG) [22]. This protein has the ability to bind estradiol , testosterone and 5-dehydrotestosterone .

Thus, in thyrotoxicosis, an increase in the concentration of thyroid hormones leads to an eightfold increase in the concentration of TESH. Accordingly, an increase in the hormone-binding capacity of plasma causes a decrease in the rate of metabolic clearance (the time for testosterone removal from the body is 50% of the norm), an increase in the total concentration of testosterone in plasma and an acceleration of its conversion to androstenediol . In this case, as a rule, clinical signs of hyperagandrogenism are not observed, since the above hormones are in a bound state due to the high level of TESH.

This condition is accompanied by activation of the extragonadal conversion of testosterone to androstenediol , androstenediol to estrone and estrone to estradiol . The resulting hyperestrogenemia via a feedback mechanism leads to a decrease in FSH concentration. Under conditions of FSH deficiency, the sensitivity of ovarian tissue to LH decreases, which leads to a decrease in progesterone levels. A decrease in progesterone, in turn, leads to an increase in LH secretion. An increase in LH levels is also facilitated by a decrease in free testosterone levels. Such a combined increase in the level of estrone and etradiol against the background of a decrease in the level of progesterone in hyperthyroidism leads to the development of proliferative processes in target organs, oligo- and opsomenorea , dysfunctional uterine bleeding [14, 16, 19, 21, 22, 34, 35].

In the mammary gland, a decrease in the antiestrogenic effect of progesterone in combination with hyperestrogenemia also leads to proliferative changes. Of interest is the fact that, despite the frequent presence of mastopathy in women with thyrotoxicosis, it is characterized by a relatively benign course with a predominance of diffuse forms in combination with leveling and even often a complete absence of clinical manifestations of mastopathy after relief of hyperthyroidism.
At In hypothyroidism, under conditions of thyroid hormone deficiency, the level of TESH decreases and, accordingly, the SMC of testosterone increases. As a result, the conversion of androstenediol is accelerated V testosterone and then testosterone into estradiol . With hypothyroidism, the metabolism of estradiol also changes : instead of normal 2-hydroxylation with the formation of active catechol estrogens , predominantly 16-hydroxylation occurs with the formation of estriol . Estriol , being the least active estrogen fraction, does not provide an adequate feedback mechanism in the regulation of gonadotropin secretion, which leads to a decrease in the concentration of LH and FSH. Clinically, this is manifested by chronic anovulation , dysfunctional bleeding, or even the development of hypogonadotropic amenorrhea in hypothyroidism. On the part of the mammary gland, this condition, accompanied by progesterone deficiency against the background of relative hypoestrogenemia (decrease in the level of metabolically active estrogen fractions), leads to the development of involutive processes associated with both changes in the state of receptors for sex steroids and with the characteristics of local hormonogenesis [10, 14, 16, 19, 21, 22, 25, 27, 34, 35].

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It was stated above that the effect of prolactin on breast tissue reaches its maximum when the level of estrogens and progestins decreases. Thus, with hypothyroidism, one can expect the summation of two effects: a change in prolactin secretion due to central mechanisms and the formation of a background of greatest sensitivity to hyperprolactinemia due to a deficiency of sex steroids.

The mechanisms of desynchronization of sex steroid synthesis in hypothyroidism are similar to those in perimenopause. It is known that it is during this period that more than 60% of breast cancer cases are detected. Taking this into account, it can be argued that the hypothyroid state, as a unique model of hormonal changes in the reproductive system characteristic of menopause, is more dangerous from the point of view of malignant degeneration in breast tissue than hyperthyroidism.

In addition to the fact that disruption of the functional activity of the thyroid gland acts as a kind of trigger for the development of pathological changes in the reproductive system and thereby contributes to the development of dishormonal processes in the mammary gland, a number of other mechanisms of the possible influence of altered thyroid status on the formation of mastopathy can be identified.

Thus, hormonal changes in hypothyroidism, leading to an increase in body weight, the development of insulin resistance and hyperinsulinemia, contribute to the development of mastopathy, which is associated with the stimulating effect of insulin, which has its own receptors on the epithelial cells of the lobules and stimulates their proliferation [17, 29].

It is possible that the influence of the level of thyroid hormones on the condition of the mammary glands can be carried out through the central and autonomic nervous systems. There is evidence that sympathicotonia , characteristic of hypothyroidism, as an adaptive response to a decrease in the level of stress hormones, contributes to an increase in the severity of the pathological process in the mammary gland [17].

According to a number of authors [39, 40], one of the metabolic aspects of the interaction between The thyroid and mammary glands are responsible for the peripheral exchange of iodine and thyroid hormones. Experimental evidence shows the ability of iodine and an iodine-rich diet to protect against breast tumor development, as demonstrated by the markedly lower incidence of breast cancer among Japanese women whose diets are rich in iodine-containing seafood. On the other hand, it is in areas with a sufficient supply of iodine that a more favorable situation is observed, in terms of the prevalence of thyroid pathology. Although there is no direct evidence, there is an opinion that it is iodine, iodinated components or a combination of iodine and selenium, which is part of antioxidant enzymes, that is the element of the Japanese diet that has a protective antitumor effect [39, 40].

Basic studies examining the role of iodine and peripheral thyroid hormone metabolism in the mammary gland have shown decreased expression of 5-deiodinase type 1 (D-1) in breast cancer cells. Type 1 (D-1) and type 2 (D-2) 5-deiodinases catalyze the peripheral conversion of the thyroid prohormone thyroxine to its active form, triiodothyronine . Normally, D-1 expression occurs in organs such as the liver, thyroid gland and lactating mammary gland. The production of this enzyme is regulated in an organ-specific manner by multiple factors such as carbohydrates, triiodothyronine , thyrotropin , and catecholamines. However, experimental studies have shown that in some types of breast cancer, D-1 expression is reduced, lost, or regulated by other components. When studying the expression and regulation of 5-deiodinases in two lines of malignant cells - MCF-7 (sensitive to the action of ovarian hormones) and MDA-MB-231 (insensitive to the action of ovarian hormones) - it was revealed that MCF-7 cells are characterized by active expression D-1 (approximately 10 pmol I(–)/mg protein per hour), which is stimulated by the administration of retinol acetate (vitamin A), but not triiodothyronine or a ® - adrenergic agonist isoproterenol . In MDA-MB-231 cells, deiodinase activity was not affected by any of the above treatments. The results obtained support the assumption that D-1 expression may be a differential marker of estrogen-sensitive malignant breast tissue [33].

Recently, a number of studies have been conducted to study the expression of receptors for the Na (+)/I(–) symporter (NIS) on infiltrating ductal breast cancer cells. The function of this membrane protein, which is a mediator of iodine transport into cells, has been well studied for the thyroid gland. NIS is also found in lactating breast cells and breast cancer tumor cells. Among the examined 50 patients with invasive ductal breast cancer, NIS expression was detected in 45 (90%) cases [37]. Perhaps further study of the mechanisms of peripheral metabolism of iodine and thyroid hormones in breast tissues that have undergone malignant degeneration will make it possible to understand more subtle pathogenetic mechanisms of the formation of combined pathology and find new approaches to diagnosis and treatment.

In studies aimed at determining the prevalence of various thyroid pathologies among patients with breast cancer compared with the control group, a significant predominance of both autoimmune diseases (38 vs. 17%, $p = 0.001$) and non-autoimmune diseases was revealed thyropathies among patients with malignant neoplasms in the mammary gland (26 vs. 9%, $p = 0.001$). The average level of antibodies to thyroid peroxidase was noticeably higher in the group of breast cancer patients compared to the control group ($p = 0.030$), which allows us to consider autoimmune damage to the thyroid gland as an increased risk factor for malignant degeneration of the hyperplastic process in the breast epithelium [41].

Analyzing the literature data on the problem of searching for the relationship between pathological conditions in the thyroid and mammary glands, the lack of a single point of view and sometimes ambiguous data from reports on research on this topic become obvious. Thus, in one of the studies [36], various combinations of pathological conditions of the mammary and thyroid glands were studied in 120 women. Women in menopause were excluded from the study; all patients had a

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regular menstrual cycle. The examination was carried out in the early follicular phase of the menstrual cycle and included an ultrasound examination of the mammary and thyroid glands with determination of the structure and volume of these organs, as well as hormonal studies. The data obtained were compared with the results of a study of a group of healthy women of similar age. Among patients with malignant breast lesions in combination with thyroid cancer, a study of hormonal status revealed a greater prevalence of subclinical hypothyroidism or a combined increase in the average levels of free T_3 and T_4 and a decrease in TSH levels (which is characteristic of hyperthyroidism) than in the control group. In the second group, represented by patients with breast cancer and any non-malignant lesions of the thyroid gland, a decrease in the average level of TSH and an increase in the average level of free fractions of thyroid hormones was detected compared to the control group. In the third group, consisting of patients with thyroid cancer in combination with benign breast diseases, a slight increase in prolactin levels was noted compared to control results. Patients with any non-malignant diseases of the mammary and thyroid glands, who made up the fourth group, were characterized by a sharp change in estrogen levels, often below the average level in the control group [36].

Another study compared the results of a thyroid examination in 97 patients diagnosed with breast cancer (first group), 61 patients with mastopathy (second group) and 60 healthy women who made up the control (third) group. Thyroid enlargement was detected in 47, 49 and 22%, respectively. Treatment with thyroid hormones was received by 9.2% (first group), 8.2% (second group) and 5.0% (third group) of patients. The level of thyroid-stimulating hormone in patients with breast cancer was noticeably higher - (5.4 ± 2.2) μmol / ml than in the group with benign breast diseases (3.9 ± 1.9; $p < 0.01$) and in group of healthy women (4.0 ± 1.8; $p < 0.001$). The level of antibodies to thyroid peroxidase (Ab to TPO) exceeded the norm in 13.4% of women in the first group, in 9.1% in the second group and in 1.7% in the third group. The levels of serum triiodothyronine and thyroxine did not differ significantly in all groups of women examined. The results of this study confirm the existence of a certain, albeit nonspecific, relationship between the presence of thyroid pathology in patients and the development of both mastopathy and breast cancer. There is a tendency towards greater severity of proliferative changes in the mammary gland in patients with autoimmune diseases. thyroiditis in a state of hypothyroidism [31].

Similar results, indicating the influence of the functional state of the thyroid gland on the formation of mastopathy, were presented in a study of the levels of T4 , TSH and prolactin in patients with mastopathy compared with the control group. Despite the fact that all the examined women were clinically in a euthyroid state, the level of thyroxine in patients with mastopathy was noticeably lower - (78.25 ± 15.27) ng / ml than in the group of healthy women (88.73 ± 15.27) ng /ml. Levels of thyroid-stimulating hormone and prolactin in women with mastopathy were characterized by a slight increase. This study also demonstrated that changes in thyroid status toward hypothyroidism are accompanied by a tendency toward pathological proliferation in the mammary epithelium [42].

Thus, various disturbances in hormonal status in women with thyroid pathology can lead to changes in the state of the receptor system in the mammary glands and the development of dyshormonal hyperplasias in them. The severity of proliferative changes does not always correlate with the severity of thyroid dysfunction. Even subclinical forms of thyroid status disorders can lead to pathological changes in the lobular-alveolar structures of the mammary gland, which will have certain clinical manifestations. At the same time, one can expect a tendency for the severity of these changes to increase when a larger number of regulatory factors (hormonal, metabolic, neurological, etc.) are involved in the process of their formation, which dictates the need for further study of this issue.

LITERATURE

1. *Balabolkin M.I., Klebanova E.M., Kreminskaya V.M. Differential diagnosis and treatment of endocrine diseases: Guide. M.: Medicine, 2002. 752 p.*
2. *Diseases of the thyroid gland: Trans. from English / Ed. L.I. Braverman . M.: Medicine, 2000. 432 p.*
3. *Burdina L.M. The influence of neuroendocrine pathology on the condition of women of reproductive age // Mammology. 1999. No. 1. P. 28–42.*
4. *Bukhman A.I. Characteristics of the condition of the mammary glands in endocrine patients before and after treatment // Mammology. 1995. No. 4. P. 17.*
5. *Gilyazutdinov I.A. Benign tumors of the mammary glands // Mammology. 1999. No. 2. P. 4–7.*
6. *Gilyazutdinov I.A., Khamitova G.V. Dyshormonal diseases of the mammary glands // Mammology. 1998. No. 4. pp. 15–19.*
7. *Gilyazutdinov I.A., Khasanov R.Sh. Tumors of hormone-dependent and hormone-producing organs. M.: MEDpress-inform , 2004. 464 p.*
8. *Dilman V.M. Endocrinological oncology: A guide for doctors. 2nd ed., revised . and additional L.: Medicine, 1983. 408 p.*
9. *Kulakova V.I. Practical gynecology: Clinical lectures. 2nd ed. / Ed. V.N. Prilepskoy . M.: MEDpress-inform , 2002. 720 p.*
10. *Levchenko I.A., Fadeev V.V. Subclinical hypothyroidism: Literature review // Problems of endocrinology. 2002. No. 2.*
11. *Letyagin V.P. Mastopathy // Rus . m units magazine 2000. T. 8. No. 11.*
12. *Makarenko N.P. Mastopathy: Lecture // Rus . m units magazine 1999. T. 7. No. 10.*
13. *Ommyanskaya A.I. Differential diagnosis and treatment tactics for dyshormonal mammary hyperplasia // Mammology. 1993. No. 2. pp. 22–23.*
14. *Potin V.V., Yukhlova N.A., Beskrovny S.V. Pathology of the thyroid gland and the female reproductive system // Problems of endocrinology. 1989. No. 1. P. 44–48.*
15. *Practical gynecology: Clinical lectures. 2nd ed. / Ed. acad. RAMS V.I. Kulakova and prof. V.N. Prilepskoy . M.: MEDpress-inform , 2002. 720 p.*
16. *Reproductive endocrinology: In 2 vols.: Transl. from English / Ed. S.S.K. Jena, R.B. Jaffe . M.: Medicine, 1998. 704 p.*

ISSN (Online): 2455-3662
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17. *Guide to Clinical Endocrinology / Ed. N.T. Starkova. St. Petersburg : Peter, 1996. 544 p.*
18. *Serov V.N., Prilepskaya V.N., Pshenichnikova V.N. Practical guide to gynecological endocrinology. M.: Rusfarmamed , 1995. 457 p.*
19. *Sosnova E.A., Laricheva I.P. Hormonal relationships in the pituitary-ovarian system in patients with hypothyroidism and diffuse toxic goiter // Obstetrics and gynecology. 1990. No. 4. pp. 38–42.*
20. *Starkova N.T., Surkov S.I., Nazarov A.N. and others. Functional state of the hypothalamic-pituitary system in euthyroid hyperplasia of the thyroid gland // Problems of endocrinology. 1991. No. 3. P. 6–7.*
21. *Tatarchuk T.F., Efimenko O.A., Ros N.V. Dyshormonal diseases of the mammary glands in the practice of a gynecologist-endocrinologist // Endocrine . gynecology. Kiev: Zapov i t , 2003. pp. 147–180.*
22. *Tatarchuk T.F., Kosey N.V., Islamova A.O. Thyroid homeostasis and dishormonal disorders of the female reproductive system // Endocrine . gynecology. Kiev: Zapov i t , 2003. pp. 147–180.*
23. *Temperman J. , Temperman H. Physiology of metabolism and the endocrine system. M.: Mir, 1989. pp. 274–314.*
24. *Tikhomirov A.L., Lubnin D.M. Local hormonal drugs in the treatment of benign breast diseases accompanied by mastalgia // Rus . m units magazine 2000. T. 8. No. 18.*
25. *Totoyan E.S. Reproductive function of women with thyroid pathology // Obstetrics and Gynecology. 1994. No. 1. pp. 8–11.*
26. *Troshina E.A., Abdulkhabirova F.M. Euthyroid pathology syndrome // Problems of endocrinology. 2001. T. 47. No. 6.*
27. *Urbanovichius V.Yu., Danis Yu.K., Nekrasova L.V., Konnova E.V. Clinical features, hormonal disorders and humoral immunity in patients with autoimmune diseases thyroiditis // Problems of endocrinology. 1990. T. 36. No. 6. P. 3–7.*
28. *Chernova T.O., Kolesnikova G.S., Mudrova S.V. and others. Reaction of prolactin and TSH in functional tests in patients with primary hypothyroidism against the background of hyperprolactinemia // Problems of endocrinology. 1994. No. 1. P. 44–48.*
29. *Shikhman S.M., Yavorskaya S.D., Gonopolskaya T.L. and etc. Secerated mammary glands and galactorrhea . Barnaul, 2001.*
30. *Esedova A., Khashaeva T. State of the reproductive system in women with endemic goiter and hypothyroidism: Review of the literature // Problems of endocrinology. 1996. T. 24. No. 2. P. 46–48.*
31. *Adamopoulos DA, Vassilaros S., Kapolla N. et al. Thyroid disease in patients with benign and malignant mastopathy . Cancer [Cancer]. 1986. Jan. _ 1. No. 57 (1). P. 125–128.*
32. *Dupont WP, Page DL Risk factors for breast cancer in women with proliferative breast disease // N. Engl. J. Med. 1997. No. 312. R. 146–451.*
33. *Garcia-Solis P., Aceves C. 5'Deiodinase in two breast cancer cell lines: effect of triiodothyronine, isoproterenol and retinmcoids // Mol. Cell . Endocrinol . 2003. Mar. _ 28.201 (1–2). R. 25–31.*
34. *Gerhard I., Betteridge J., Holder R. et al. Thyroid and ovarian function in infertile women // Hum. Reprod . 1991. No. 6. R. 338.*
35. *Inzucchi Silvio E., Burrow Gerald N. The thyroid gland and reproduction // Reproductive Endocrinology. Philadelphia : WB Saunders , 1999, pp. 413–435.*
36. *Parmeggiani D., Malinconico F. A., Moccia G. et al. Hormonal therapy in oncologic treatment: pathogenic hypotheses and interactions between thyroid and breast pathologies. Tumori . 2003. Jul-Aug . 89 (Suppl . 4). P. 215–219.*
37. *Rudnicka L., Sinczak A., Szybinski P. et al. Expression of the Na(+)/I(–) symporter in invasive ductal breast cancer // Folia Histochem . Cytobiol . 2003. No. 41(1). R. 37–40.*
38. *Russo J., Russo IH Role of hormones in human breast development: the menopausal breast. Menopause Biology and Pathobiology / Ed by RA Lobo et al. New York , 1996, pp. 184–193.*
39. *Smyth PP Role of iodine in antioxidant defense in thyroid and breast disease // Biofactors . 2003. No. 19 (3–4). R. 121–130.*
40. *Smyth PP The thyroid, iodine and breast cancer // Breast. Cancer Res. 2003. No. 5(5). R . 235–238. Epub . 2003 Jul. 29.*
41. *Turken O., NarIn Y., DemIrbas S. et al. Breast cancer in association with thyroid disorders // Breast. Cancer Res . 2003. No. 5(5). R. 110–113. Epub . 2003 Jun . 05.*
42. *Zych F., Mizia-Stec K., Mucha Z., Zych-Twardowska E. Fibrocystic disease of breast and pituitary-thyroid axis function // Pol. Merkuriusz Lek . 1996. Oct. _ No. 1 (4). P. 227–228*